ARCHIVES OF SURGERY

VOLUME 13 OCTOBER, 1926 NUMBER 4

SURGERY OF THE LUNG

EXPERIMENTAL LOBECTOMY AND PNEUMECTOMY *

S. A. SCHLUETER, M.D.
AND
I. F. WEIDLEIN, M.D.
CLEVELAND

Our interest in lobectomy and pneumectomy was derived from a desire to remove lobes from dogs in which we had established lung abscesses [1] for the purpose of studying the lesion at various stages of development without killing the animal. In a review of the literature on this particular subject, one certain method was chosen which to us seemed to embody correct surgical principles and to which we have added several refinements in technic. The added danger of an abscessed lung with which we were confronted necessarily submitted the method to an unusually severe test in comparison with the experimental work of others in which normal dogs were used. Nevertheless, our results proved highly satisfactory.

Lobectomy and pneumectomy received their first scientific experimental investigation in 1881 when Gluck [2] removed one entire lung in six dogs and fourteen rabbits. With the exception of two rabbits all of the animals died in between seven and ten days with pleuritis and pericarditis. The following conclusions were drawn: The operative procedure is well tolerated; the stump lives and forms part of the cicatrix; with careful asepsis healing will take place and no serious results will occur. Marcus [3] in 1881 experienced similar results. Independently of Gluck, Schmid [4] likewise performed experiments in lung surgery. In eight partial apical resections in dogs, there were five deaths

* From the Laboratory of Surgical Research, the Lakeside Hospital and the Western Reserve University School of Medicine.

1. Schlueter, S. A., and Weidlein, I. F.: Postoperative Lung Abscess: An Experimental Study, to be published.

2. Gluck, T.: Experimenteller Beitrag zur Frage der Lungen-exstirpation, Berl. klin. Wchnschr. **18**:645, 1881.

3. Marcus, quoted from Murphy, J. B.: Surgery of the Lung, J. A. M. A. **31**:151 (July 23); 208 (July 30); 281 (Aug. 6); 341 (Aug. 13) 1898.

4. Schmid, H.: Experimentelle Studien über partielle Lungenresektion, Berl. klin. Wchnschr. **18**:757, 1881.

and three recoveries. Four of the deaths resulted from suppurative pleuritis and one from acute phenol (carbolic acid) poisoning. Block's [5] experiments were discouraging. All of the animals operated on, five rabbits and four dogs, died from a septic pleurisy. Even in other experiments in which single lobes were removed from dogs, only two animals recovered. The researches of Biondi [6] in 1882 were more successful and were the best obtained in these early investigations. Tubercle bacilli were injected into the lung with the hope of producing localized pulmonary tuberculosis. Rabbits, cats and dogs were used. In eleven total extirpations of one lung, four died from a septic pleuritis. The results of Zakharevitch [7] in 1890 equaled those of Biondi. He experimented on thirteen rabbits and eleven dogs. Two operations on rabbits and three on dogs were fatal. Mass ligation at the root of the lung was done with silk and iodoform was applied to the stump. In 1891 Willard [8] performed a successful experimental pneumectomy in one dog by suturing the stump, ligated *en masse,* into the wound. The disastrous results experienced by the first investigators were likewise experienced by Murphy [9] in 1898. In a series of nine dogs in which pneumectomy was performed, there was only one recovery. Eight dogs died soon after the operation, usually from a septic pleuritis.

With the exception of the results obtained by Biondi and Zakharevitch, these early experimental lung resections were successful in only a small percentage of the experiments. They served, however, to show that the removal of a lung by ligating the hilum was possible, and that no dangerous sequelae arose if the element of infection was avoided.

Green [10] resected parts of the lung in fourteen dogs. Seven developed a septic pleuritis. Tiegel [11] considered mass ligation a primitive method. In three dogs in which this method was employed, the bronchus reopened after four days, eight days and three weeks, respectively. In other dogs simple ligation of the isolated bronchus resulted in pressure necrosis and a reopening of the lumen after from two to three days.

Because of such poor results Tiegel developed the following technic: A mass ligature of silk was placed about the hilum (catgut is absorbed

5. Block: Experimentelles zur Lungenresektion, Deutsche med. Wchnschr. **7**:634, 1881.

6. Biondi, D.: Lungenexstirpation bei experimenteller lokalisirter Tuberculose, Wien. med. Jahrb., 1884, p. 207.

7. Zakharevitch, quoted by Willard, DeForest: Experiments in Pneumonectomy and Pneumonotomy, Tr. Coll. Phys. **13**:133, 1891.

8. Willard (footnote 7).

9. Murphy (footnote 3).

10. Green, N. W.: The Positive Pressure Method of Artificial Respiration, Surg. Gynec. Obst. **2**:512, 1906.

11. Tiegel, M.: Experimentelle Studien über Lungen- und Pleurachirurgie, Mitt. a. d. Grenzgeb. d. Med. u. Chir., supplement 3, 1907, p. 789.

too rapidly); the ligature was purposely tied loosely to prevent necrosis; the vessels were ligated again peripherally; the lobe was removed, leaving a small amount of lung tissue about the hilum which was sutured over the stump; the bronchial stump lumen was first curetted and ligated distally to the first loose ligature. The method was used in seventeen dogs. No data concerning the postoperative result were given. Robinson [12] resected the entire right lung from dogs with the aid of positive pressure with a high percentage mortality. Danielsen [13] concluded from his experiments that it was possible to close a bronchus so that it would remain closed. In six dogs the main bronchus was opened and then closed with silk. The animals all lived and the bronchus remained closed. In four other dogs a portion of one lobe also was resected. There were no deaths. In twenty-one consecutive thoracotomies performed by Halsted,[14] there was only one primary infection of the pleura. These results contrasted markedly with the previous experimental reports. The method used in treating the bronchial stump was as follows: The isolated bronchus was bisected and the mucous membrane removed. The two halves of the bronchus were flattened together and held with a series of sutures around the edges, together with interrupted through-and-through sutures which encircled the cartilages.

The results of Biondi's experiments were never realized until 1909 when Meyer [15] described the *inversion method of treating the bronchial stump*. The method used was as follows: The main bronchus was isolated, crushed and ligated with a transfixing ligature of medium silk. The stump was cauterized and inverted by purse string sutures. This method has given the best results in the hands of all who have attempted experimental lung surgery. Twenty-one total excisions of one lung were performed on dogs with only four deaths. In only one case death resulted from a leaky bronchial stump. In five other dogs a lobectomy was performed. All the animals recovered. Robinson and Sauerbruch [16] removed one lung in thirty-eight animals. There were only four recoveries. Although the authors attributed their bad results to the positive pressure employed, death, no doubt, resulted from pleural infection and bronchial stump leakage. The pleural effusion was believed to be a

12. Robinson, S.: Experimental Surgery of the Lung: I. Thirty Animal Operations Under Positive Pressure, Ann. Surg. **47**:184, 1908.

13. Danielsen, W.: Beitrage zur Lungenchirurgie: Bronchotomie und Lungenresektion, Beitr. z. klin. Chir. **60**:94, 1908.

14. Halsted, W. S.: Clinical and Experimental Contribution to the Surgery of the Thorax, Tr. Am. S. A. **27**:119, 1909.

15. Meyer, W.: Pneumectomy with the Aid of Differential Air Pressure: An Experimental Study, J. A. M. A. **53**:1978 (Dec. 11) 1909.

16. Robinson and Sauerbruch: Untersuchungen über die Lungenextirpation unter vergleichender Anwendung beider Formen des Druckdifferenze varfahrens, Deutsche Ztschr. f. Chir. **102**:542, 1909; Zentralbl. f. Chir. **37**:391, 1910.

transudate and not infected. Simple ligation of the hilum was all that was done. The results of Schlesinger [17] were similarly poor. One lung was removed from seventeen dogs. Only five lived. The bronchial stump was doubly ligated with silk and covered over with a fold of pericardium. In the opinion of Quinby and Morse [18] the method of Meyer seemed the most accurate and successful. Thirty-eight pneumectomies were performed on dogs with only eight deaths. The difficulty of pushing in a large crushed portion of the main bronchus on the right side was met by treating each of the primary bronchi separately.

In 1914 Henschen [19] suggested the procedure of introducing a roll or plug of fascia into the lumen of the divided bronchus and closing the stump over it. The problem was undertaken experimentally by Giertz,[20] but the method was modified somewhat in that the crushed bronchial stump was first sutured with silk mattress sutures and then covered with small fascial transplants sutured with silk to the peribronchial tissues. This was in turn covered with pleura and pericardium. Ten large dogs were operated on. There were no pleural infections and only two fatalities from "Spannungspneumothorax." Kawamura [21] removed one lung from twenty-three dogs. The method as devised by Tiegel was usually employed, but without the proximal bronchial ligature. He concluded that the method of Willy Meyer was not always possible if the bronchial stump was too short. In only six cases could this method be carried out. There were only two dogs in which death was caused by leakage from the bronchial stump. Similar good results were obtained by Heuer and Dunn.[22] Of the twenty-three dogs operated on there were thirteen recoveries and ten deaths. Six deaths were due to distemper and only two of the dogs died from an acute pneumothorax because of an intentionally poor closure of the bronchial stump. All the various methods previously attempted were tried and good results

17. Schlesinger, A.: Experimentelle Untersuchungen über Lungenoperationen unter inter thorakaler Insufflation, Verhandl. d. deutsch. Gesellsch. f. Chir. 40 Kong. **2**:448, 1911.

18. Quinby, W. C., and Morse, G. W.: Experimental Pneumectomy: The Application of Data So Obtained to the Surgery of the Human Thorax, Boston M. & S. J. **165**:121, 1911.

19. Henschen, K.: Experimente zur intrathorakalen Lungenchirurgie, Beitr. z. klin. Chir. **90**:373, 1914.

20. Giertz, K. H.: Ueber Exstirpation von Lungen und Lungenlappen mit Versorgung des Bronchialstumpfes durch frei transplantierte Fascia lata, Zentralbl. f. Chir. **41**:1433, 1914.

21. Kawamura, K.: Experimentelle Studien ueber die Lungenexstirpation, Deutsche Ztschr. f. Chir. **131**:189, 1914.

22. Heuer, G. J., and Dunn, G. R.: Experimental Pneumectomy, Bull. Johns Hopkins Hosp. **31**:31 (Feb.) 1920.

were obtained. Bettman [23] experienced a high percentage of failures after both simple lobectomies and pneumectomies. In the latter group, twenty-seven dogs were operated on. All except two died from pleural infection and sloughing of the bronchial stump. He concluded that the closing of a bronchus was difficult on account of the "inherent inertness" of the bronchial wall tissue.

An analysis of the previous results of experimental lobectomy or pneumectomy reveals one outstanding fact, the high incidence of pleural infection after operation. Indeed, it appears that this complication is the only factor that has never been entirely prevented even though numerous procedures have been advocated toward securing a permanent closure of the bronchial stump.

The various types of operations do not emphasize the very important rôle that infection plays once bacteria are introduced into the bronchial stump tissues. In these operations, which were limited almost entirely to normal, healthy animals without preexisting lung disease, infection undoubtedly originated from within the bronchial lumen because sufficient care was not taken to prevent bacterial contamination of the stump or tissues about the stump. The bacteria having established themselves in the bronchial stump tissue—a tissue whose local resistance to infection is low—access to the mediastinal tissues and to the pleural membranes was easily gained and a fatal septic pleuritis resulted. Infection of the pleura does not necessarily imply a necrosis and a reopening of the bronchial lumen. Either may occur independently of the other. Obviously, in the methods in which the bronchial lumen is opened, in which various plastic operations are performed on the stump and in which the suture material passes through the infected lumen, infection cannot be avoided. Infection may likewise arise from without the bronchial lumen and in particular from an improperly cauterized stump. Apparently, the final operative result is in a great part dependent on the presence or absence of infection as emphasized by Carrel [24] since sufficient experimental work has already been done to demonstrate that an entire lung can be removed without disturbing the well-being of the animal.

Although it is important to prevent the introduction of infection into or about the tissues of the bronchial stump, it seems just as important to treat the stump with meticulous care. Of the different methods described, that method which least disturbs the anatomic relations at the hilum and which attempts to maintain the normal continuity of struc-

23. Bettman, R. B.: Experimental Closure of Large Bronchi: A Study of the Factors Concerned in Failure of the Bronchi to Heal, Arch. Surg. **8**:418 (Jan.) 1924.

24. Carrel, A.: The Technique of Intrathoracic Operation, Tr. Am. S. A. **32**:451, (discussion) 483, 1914.

tures is the method of choice. The rigid cartilaginous rings continually tend to separate the opposed bronchial walls and if the meager blood supply of the bronchus is interfered with by rough and careless handling of the stump necrosis of the tissues and a reopening of the lumen is sure to follow, thereby establishing a sudden, direct communication between the air passages and the pleural cavity.

The bronchus is composed mainly of cartilaginous tissue, a tissue that is prone to undergo degenerative changes when subjected to slight traumatic injury. A poor blood supply increases the existing tendency of such structures toward degeneration and failure to participate in a reparative process. Even a slight degree of trauma to the vascular structures about the bronchus may, therefore, interfere sufficiently with the blood supply to hinder or prevent healing. In any operation on the bronchus, great care must be taken not to dissect away and destroy too much of the peribronchial tissue for this tissue contains the blood vessels supplying the bronchial wall. The freeing of the bronchus from its enveloping connective tissue seems to have been an important factor in the failures of many investigators.

Briefly, the ideal procedure would seem to be one in which the element of infection could be eliminated, and in which manipulations and traumatisms of the stump are reduced to a minimum. In our opinion successful removal of a lobe or lobes is dependent solely on the technic that will insure an aseptic air-tight closure of a divided bronchus. The invagination method, originally proposed by Meyer, with certain added modifications, we believe, meets such requirements. The method attempts to simulate the technic used in an appendectomy and is as follows:

METHOD

The dog is given a preliminary injection of one-sixth or one-fourth grain (0.01 or 0.016 Gm.) of morphine and anesthetized with ether administered by a cone. After anesthesia is complete, the animal is placed on the right or left side, depending on whether the left or right pleural cavity is to be entered. A rubber tube, slightly smaller in diameter than the inside diameter of the trachea, is then inserted into the trachea and connected to an apparatus [25] for interrupted insufflation anesthesia. The thorax is shaved and the skin cleansed with soap, water, alcohol and mercuric chloride (1 : 3,000 solution). Sterile drapings are placed about the proposed incision and the entire procedure is carried out with a careful aseptic technic. An incision is made through the skin

25. We have used the Erlanger double cylinder apparatus, by means of which air mixed with varying amounts of ether vapor is forced intermittently under slight pressure into the air passages. The air returns from the lungs through the space between the intratracheal tube and the trachea.

over and parallel to the fourth interspace extending from the sternum to the posterior axillary line. The platysma, latissimus dorsi and intercostal muscles are cut, and the parietal pleura is punctured with a blunt instrument. The pleura is incised with scissors and the wound margins are held retracted with a self-retaining retractor. A large enough opening is produced by this incision to permit easy palpation of any lobe of a

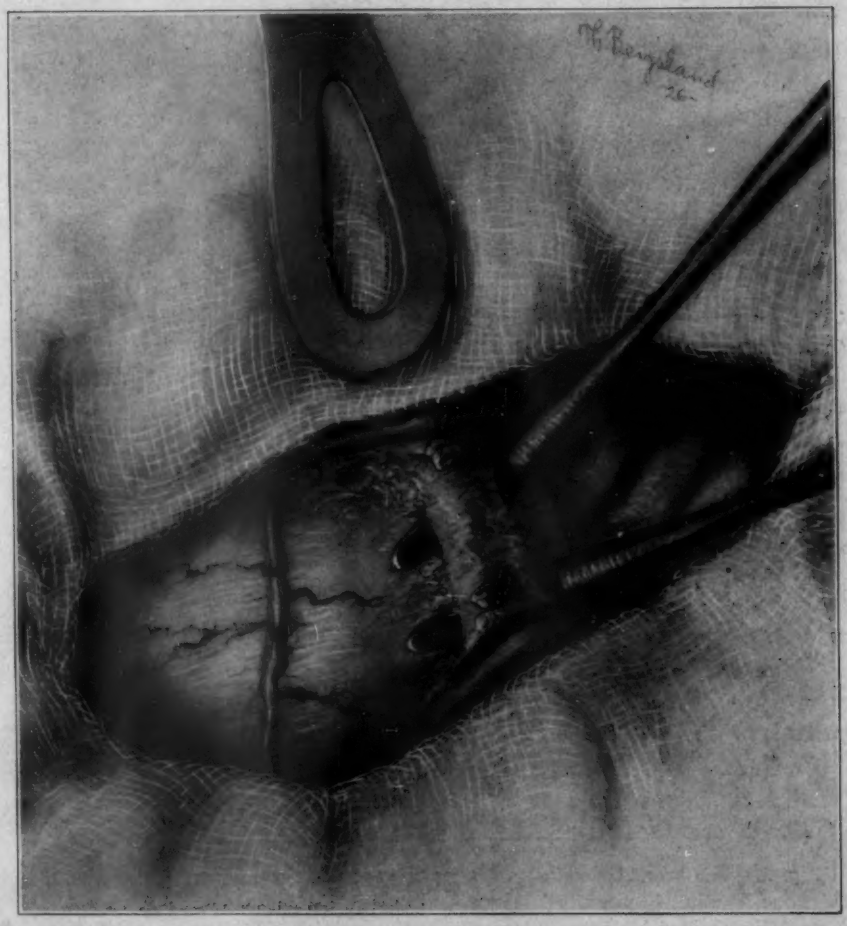


Fig. 1.—The left lower lobe hilum has been exposed; the artery has been divided between a distally placed ligature and two centrally placed ligatures; the bronchus is being isolated.

lung, and the opening in the chest wall is so situated as to allow free access to the hilum. When the pleural cavity is entered, the degree of aeration of the lungs is regulated. Regardless of whether an entire lung or a single lobe is to be removed, the first procedure consists in isolating and ligating the artery. In a pneumectomy, the main branch of the pul-

monary artery is dissected free near the base of the heart. If only the lower lobe is to be removed, the vessel is freed from the vascular sheath lateral and posterior to the bronchus (fig. 1). The artery is isolated; two silk ligatures are placed centrally; one silk ligature is placed peripherally, and the vessel is severed between ligatures. The next step consists in freeing each respective lobe bronchus. Extreme

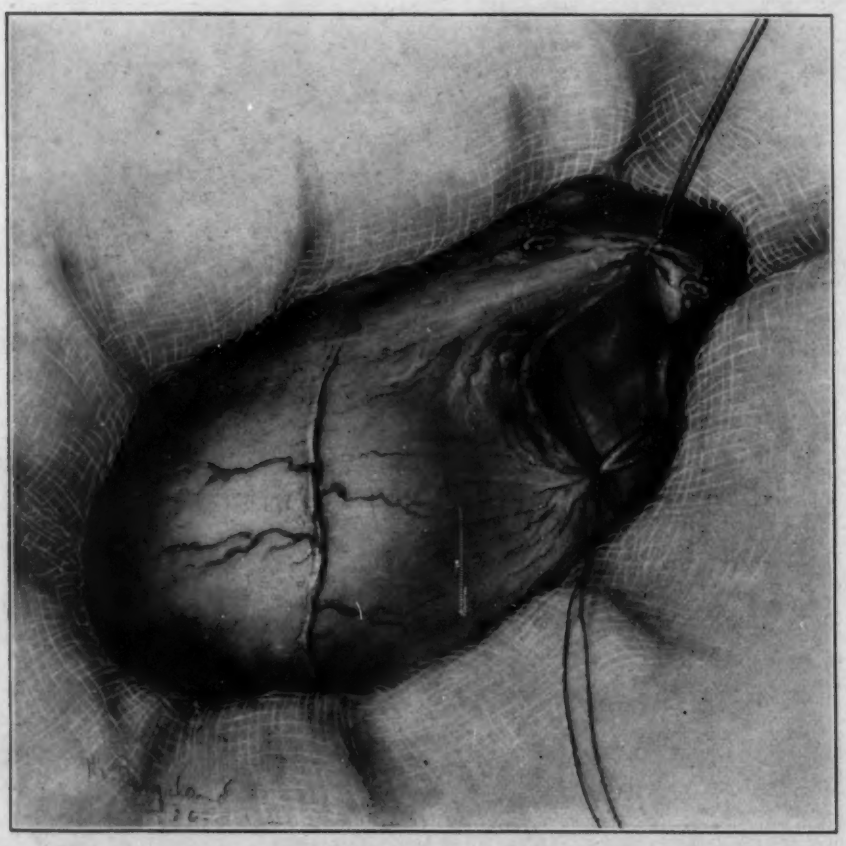


Fig. 2.—The bronchus with attached peribronchial tissues has been ligated distally; the lobe has been pushed laterally to expose the pulmonary veins which are about to be divided between ligatures.

care must be exercised not to strip away too much peribronchial tissue. The structures are carefully dissected away from the point of entrance of the bronchus into the lobe to a centrally situated point that will allow sufficient space for the placement of two ligatures. A plexus of nerve fibers, including the vagus, lies posteriorly and medially in close relationship with the bronchus so that care must be taken not to disturb these structures. While the lung is in a deflated condition, each bronchus is

ligated near the lobe with linen and the ends are left long so that the threads may be used for traction. Further manipulations of the lobe can now be carried out without the danger of spilling accumulated secretions into other parts of the bronchial tree. Likewise, the further progress of the operation is not so much interfered with after the constant refilling of the lobes with air ceases.

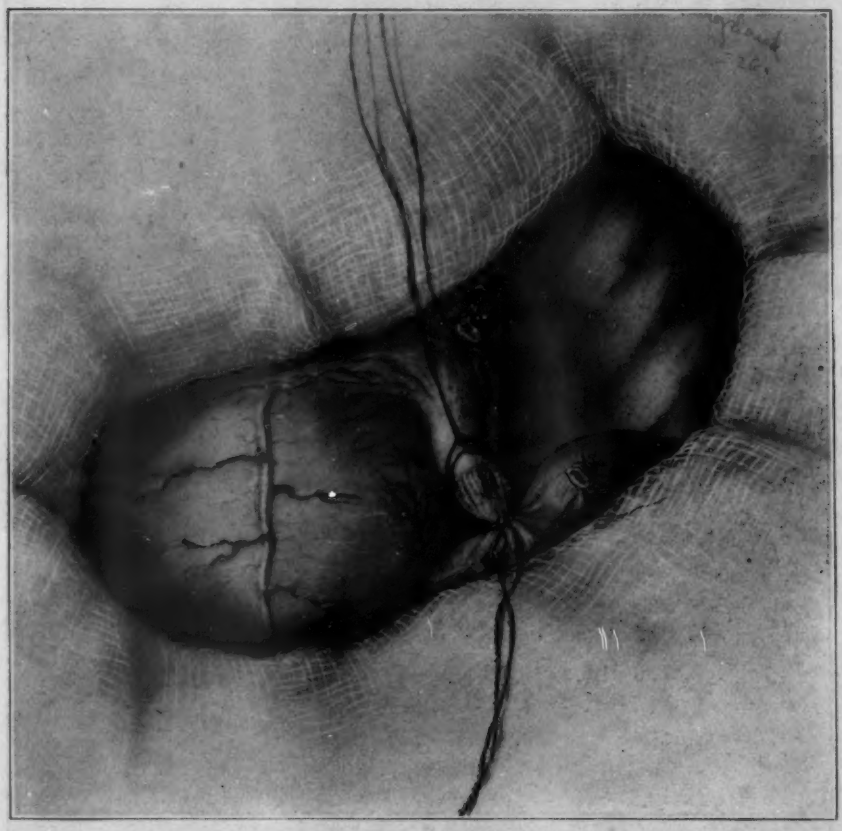


Fig. 3.—The bronchus has been crushed just central to the distal bronchial ligature; a ligature of no. 1 chromic catgut is being placed about the upper portion of the crushed area; the bronchus is then severed between the two ligatures with a knife and both stumps are cauterized with phenol and alcohol.

The lobes are now pushed laterally to bring the pulmonary veins into view (fig. 2). Two or three of these vessels emerge from each lobe and after combining into one or two larger veins pass directly toward the base of the heart. The wall of each vein is exceedingly thin and the vessel may easily be torn across during the dissection. After each vessel is ligated separately at both ends with silk, the veins are cut between the ligatures. The danger of further bleeding having thus been

eliminated, attention is directed toward treating the bronchus. At a point just proximal to the linen ligature the bronchus is crushed with a clamp and a ligature of no. 1 chromic catgut is placed about the upper portion of the crushed area (fig. 3). The ends of this ligature are left long and gauze packs are placed about the bronchus. The bronchus is

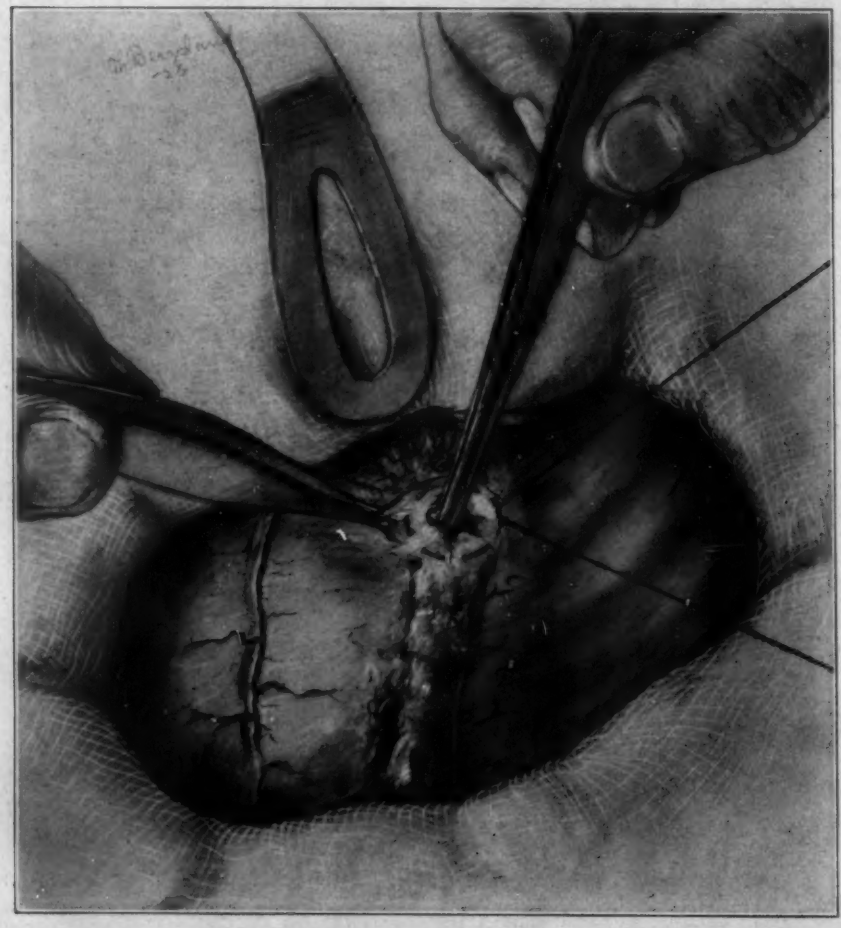


Fig. 4.—The lobe has been removed; a purse string of no. 1 chromic catgut has been placed into the bronchial wall and the stump is being invaginated.

severed with a knife between the two ligatures, the knife is discarded, and both ends of the stump are cauterized with phenol and alcohol. The gauze prevents pleural contamination. The lobe is then removed, and any pleural adhesions present are carefully separated by blunt and sharp dissection. Other lobes are similarly removed. A purse string of no. 1 or zero chromic catgut is then placed in the bronchial wall a short

distance from the stump, care being taken that the actual wall of the bronchus is included in the small needle bites *without perforating* into the lumen of the bronchus. A French needle is best adapted for this purpose. With a tooth forceps the assistant firmly grasps the bronchial

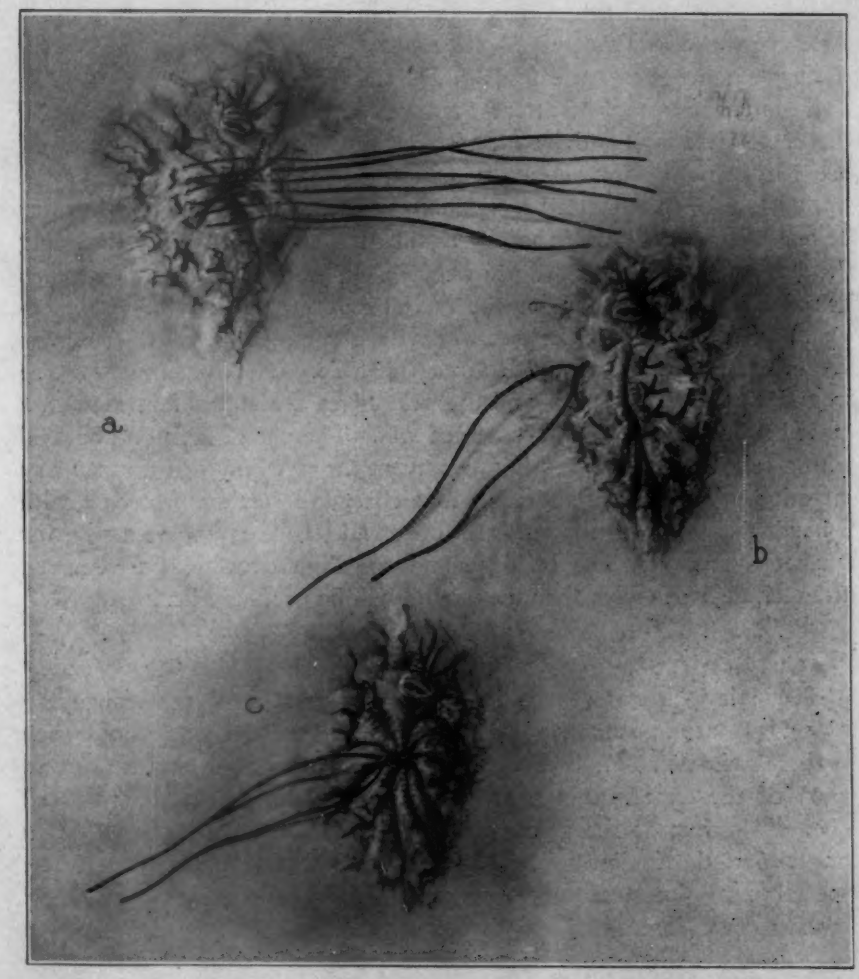


Fig. 5.—(*a*) Mattress sutures of silk have been placed into the bronchial wall across the stump; (*b*) the mattress sutures have been tied to reinforce the invagination; a purse string of silk has been placed into the peribronchial tissues; (*c*) the peribronchial tissue has been pulled over the layer of mattress sutures.

wall above the purse string at a point directly opposite the purse string knot. With these two points held anchored, the assistant invaginates the stump while the operator ties the knot (fig. 4). If the purse string is properly placed and the two fixed points are properly selected, we

believe that there should be no difficulty in invaginating any bronchial stump. We have been able to perform this procedure in every contemplated instance. In the case of a primary bronchus, the stump was easily invaginated. To further reinforce the closure, three mattress sutures of silk are also placed across the stump. These sutures are likewise placed into the bronchial wall but do not penetrate the lumen. A final purse string is placed in the loose peribronchial tissue to cover the layer of mattress sutures (fig. 5).

It is not necessary to attempt suture of the pleura. The opening in the chest wall is closed by merely placing two interrupted sutures of no. 1 chromic catgut about the upper and lower ribs bordering the wound. The sutures can be placed through holes drilled in the ribs as described by Friedrich,[26] thereby eliminating the necessity of including the intercostal vessels of the lower rib. The pleural cavity can then be made air-tight by suturing the fascial covering of the ribs and intercostal muscles. Before the pleural cavity is completely sealed, the lungs are inflated to expel as much air as possible. The remainder of the wound is sutured in layers and the skin edges are approximated with a buried subcuticular running stitch of silk. The closed incision is sealed with a collodion gauze dressing to prevent the possibility of a secondary infection. The wound and the entire chest are further protected with a bandage. If careful asepsis is observed, there is no necessity for further dressings. The bandage and collodion dressing are removed after ten days at which time the wound will be perfectly healed.

RESULTS

A single lobe was removed from twenty-four dogs (accompanying table). A septic embolus had been injected intravenously into each of these animals at some time previous to the operation, and in a great many of the experiments a lung abscess was present in the removed lobe. In a few of the animals in which the lesion had existed for a longer period of time, a healed area of fibrosis was demonstrable. Special precautions had to be observed in ligating and tying the bronchus in those operations in which we were dealing with a lobe containing a large abscess. The operative technic as described in the foregoing was not evolved until a series of experiments were performed in which various methods were employed to close the bronchial stump. There were eleven operations in which the following methods were used: (1) a mass ligation of the hilum; (2) a simple ligation of the bronchus; (3) a simple ligation of the bronchus plus a covering of peribronchial tissue, and (4) a suturing of the divided bronchus with silk. The ends of both stumps were always cauterized with phenol and alcohol.

---

26. Friedrich, P. L.: Die Chirurgie der Lungen, Arch. f. klin. Chir. **82**:1147, 1907.

Experiment	Lobes Removed	Operative Method*	Duration of Lesion	Lesion in Removed Lobe	Days Lived after Operation	Cause of Death	Condition of Bronchial Stump	Remarks
1 (Y 11)	Left lower lobe	Mass ligation at hilum; stump not cauterized	19 days	Area of fibrosis	23	Diffuse pulmonary gangrene; empyema	Healed	Wound healed by first intention; source of infection obscure
2 (Y 13)	Left lower lobe	Simple ligation.....	14 days	Two small abscesses	4	Pyopneumothorax	Bronchus open	Ligature had sloughed away
3 (Y 14)	Left lower lobe	Simple ligation.....	14 days	Area of fibrosis	87	Killed	Healed	Killed because of mange
4 (Y 27)	Right lower lobe and right middle lobe	Simple ligation.....	27 days	Small abscess	Still living			
5 (Y 45)	Right lower lobe	Simple ligation.....	12 hours	Septic embolus in artery	Still living			
6 (Y 9)	Left lower lobe	Peribronchial purse string	14 days	Small abscess	29	Bilateral empyema, cause obscure	Healed	Wound healed by first intention; dog perfectly well until a few days before death, except for mange
7 (Y 18)	Left lower lobe	Peribronchial purse string	10 days	Small abscess	Still living			
8 (Y 21)	Left lower lobe	Peribronchial purse string	33 days	Area of fibrosis	57	Diffuse pulmonary gangrene; empyema	Healed	Wound healed by first intention; source of infection obscure
9 (Y 24)	Right lower lobe	Peribronchial purse string	33 days	Fibrosis of cavity almost complete	Still living			
10 (Y 30)	Right lower lobe	Peribronchial purse string	16 days	Small abscess	31	Not determined	Healed	Lungs and pleurae normal
11 (Y 43)	Right lower lobe	Bronchus sutured with silk	18 hours	Septic embolus in artery	Still living			
12 (Y 19)	Left lower lobe	Invagination stump....	34 days	Small abscess	Still living			
13 (Y 20)	Left lower lobe	Invagination stump....	6 days	Large abscess	63	Killed	Healed	Killed because of mange
14 (Y 29)	Left lower lobe	Invagination stump....	23 days	Small abscess	23	Killed	Healed	Killed because of distemper
15 (Y 31)	Left lower lobe	Invagination stump....	23 days	Large abscess	40	Starvation (?)	Healed	Lungs and pleurae normal
16 (Y 33)	Right lower lobe	Invagination stump....	19 days	Area of fibrosis	Still living			
17 (Y 36)	Right lower lobe and right middle lobe	Invagination stump....	21 days	Large abscess	18	Distemper	Healed	Animal had distemper at time of operation; a consolidated right middle lobe also was removed
18 (Y 37)	Right lower lobe	Invagination stump....	17 days	Area of fibrosis	Still living			
19 (Y 38)	Left lower lobe	Invagination stump....	16 days	Small abscess	Still living			
20 (Y 39)	Right lower lobe	Invagination stump....	12 days	Large abscess	Still living			
21 (Y 40)	Right lower lobe	Invagination stump....	13 days	Area of fibrosis	105	Killed in fight	Healed	
22 (Y 41)	Left lower lobe	Invagination stump....	8 hours	Septic embolus in artery	2	Bronchopneumonia	Securely closed	Pleural cavities clear; wound clean; marked consolidation of right middle and left upper lobes
23 (Y 42)	Left lower lobe	Invagination stump....	4 hours	Septic embolus in artery	Still living			
24 (Y 44)	Right lower lobe	Invagination stump....	24 hours	Small abscess	4	Empyema	Securely closed	Wound slightly infected; pleural infection must have resulted from a slip in the operative technic
25 (Y 50)	Right pneumectomy	Invagination stumps...	4 days	Abscess in right lower lobe	Still living			
26 (Y 53)	Left pneumectomy	Invagination stumps...	.....	None	Still living			
27 (Y 59)	Left pneumectomy	Invagination stumps...	4 days	Abscess in left lower lobe	4	Empyema	Securely closed	Wound infected; pleura grossly infected at time of operation
28 (Y 60)	Right pneumectomy	Invagination stumps...	4 days	Abscess in right middle lobe	Still living			

* Unless otherwise noted the pulmonary vessels were ligated individually, the bronchus was ligated with no. 1 chromic catgut and sectioned between ligatures. Both stumps were cauterized with phenol and alcohol. A purse string of no. 1 chromic catgut was used in those cases in which the bronchial stump was invaginated. Silk was used for reinforcing mattress sutures and for the peribronchial purse string.

1. In the one experiment in which the hilum was ligated *en masse* with no. 1 chromic catgut, the animal lived for twenty-three days after the operation (experiment 1, dog Y 11). At necropsy a bilateral empyema and gangrenous lesions in the remaining left lung were found. The bronchial stump was healed. The source of the infection was difficult to determine, but the possibility of pleural infection by bacteria of low virulence originating from the stump at the time of the operation had to be considered.

2. In four experiments the bronchus was simply ligated with a ligature of no. 1 chromic catgut. In one animal (experiment 2, Dog Y 13) the bronchus reopened after four days and death resulted from a pyopneumothorax. Two animals (experiment 4, Dog Y 27, and experiment 24, dog Y 45) are still living and one (experiment 3, dog Y 14) was killed after eighty-seven days because of mange. The healed bronchial stump consisted of dense fibrous tissue.

3. In five experiments the ligated stump was covered with peribronchial tissue by using a purse string suture of silk. One animal (experiment 6, dog Y 9) died after twenty-nine days from a bilateral empyema and one (experiment 8, dog Y 21) after fifty-seven days from a bilateral empyema and lung gangrene. Another (experiment 10, dog Y 30) in which the cause of death could not be determined died on the thirty-first postoperative day. At necropsy no lesions of the lungs or pleura could be found. In each of these three dogs the bronchial stump was healed. It was difficult to understand why the signs of fatal pleural infection were not recognized until late in the postoperative period. The dogs seemed to be well until a few days preceding death. In each case the wound in the chest wall had healed by first intention, and, as previously discussed, the infection probably originated from bacteria of low virulence carried to and implanted on the pleura from the stump at the time of the operation. The other two animals (experiment 7, dog Y 18, and experiment 9, dog Y 24) are still living.

4. In the fourth method the severed bronchus was closed with a continuous suture of silk. The postoperative course was uneventful and the dog is still living (experiment 11, dog Y 43).

In the thirteen remaining experiments the bronchial stump was treated by the invagination method and in none of these animals did sloughing or reopening of the stump occur. Only two deaths were attributed to the operative procedure. In experiment 22, dog Y 41, death occurred on the second day following operation. At necropsy a marked consolidation of the right middle and upper lobes was found, but the pleural cavities were free from infection. Death probably resulted from a bronchopneumonia. A bilateral empyema was responsible for the second death (experiment 24, dog Y 44). The wound in the chest wall was grossly infected. The bronchial stump was securely

closed so that the pleural infection probably resulted from a break in the aseptic technic. One animal (experiment 15, dog Y 31) died forty days after operation but the cause of death was not determined. At necropsy marked emaciation was the only observation. Distemper was the cause of the death in experiment 17, dog Y 36. At the time of the production of the lung abscess the animal already had some signs of distemper, viz., cough, apathy, anorexia and a slight purulent discharge from the nostrils. At operation twenty-one days later, the right lower lobe contained a large abscess and the right middle lobe was completely consolidated. It was decided to give the operative technic a critical test, and the consolidated lobe was likewise removed. The animal was quite ill during the first few days following the operation; the nasal discharge was quite profuse and at times quite hemorrhagic. For a time, however, the general condition seemed improved, but the animal failed to overcome the infection and death occurred on the thirteenth postoperative day. At necropsy the remaining lobes of the lung showed the typical distemper conditions. Both pleural cavities, however, were free from infection and the bronchial stumps as well as the external chest wound were perfectly healed. This would seem to illustrate how the pleural cavity can be entered with perfect safety even in the presence of severe pulmonary infections if rigid aseptic technic is adhered to. The foregoing case illustrates also how entire lobes can be removed if the bronchus is recognized as being infected and is dealt with accordingly. With the exception of one animal, which was killed in a fight, the remaining animals are still living.

The following typical protocol illustrates the invagination method:

PROTOCOL

EXPERIMENT 17.—Dog Y 36, weighing 13.2 Kg., Nov. 23, 1925, was given one-fourth grain (0.016 Gm.) of morphine. Thirteen days previously a septic embolus had been freed into the jugular vein. Subsequent roentgenograms had shown a developing abscess in the right lower lobe. On the day preceding lobectomy, the right middle lobe was seen to show consolidation (fig. 6). The dog had had distemper for some time, and it was thought that the consolidated right middle lobe was a part of the disease. Under ether intratracheal insufflation the animal was anesthetized and the right pleural cavity was entered through the fourth intercostal space. Examination revealed no adhesions about the lower lobe. The middle lobe was solid and reddish with numerous white areas presenting on the surface of the lobe. The lower lobe was first removed. The pulmonary artery to the lobe was isolated, ligated and sectioned between ties. The bronchus was then isolated and ligated distally with linen. The veins were ligated distally and centrally and severed between ligatures. The bronchus was then crushed with a clamp just central to the linen ligature. A ligature of no. 1 chromic catgut was placed about the crushed area, the bronchus was cut across between the ligatures with a knife, and both stumps were cauterized with phenol and alcohol. A purse string of no. 1 chromic catgut was placed in the wall of the bronchus, and the stump was invaginated. The stump was further reinforced with three mattress

sutures of silk and a peribronchial purse string gave additional covering. The right middle lobe was similarly treated. The pleural cavity was closed with two pericostal sutures of no. 1 chromic catgut, and the wound was closed in layers with a running stitch of silk. A buried subcuticular stitch approximated the skin. The lower lobe showed a large abscess (fig. 7), and the middle lobe showed a diffuse bronchopneumonia.

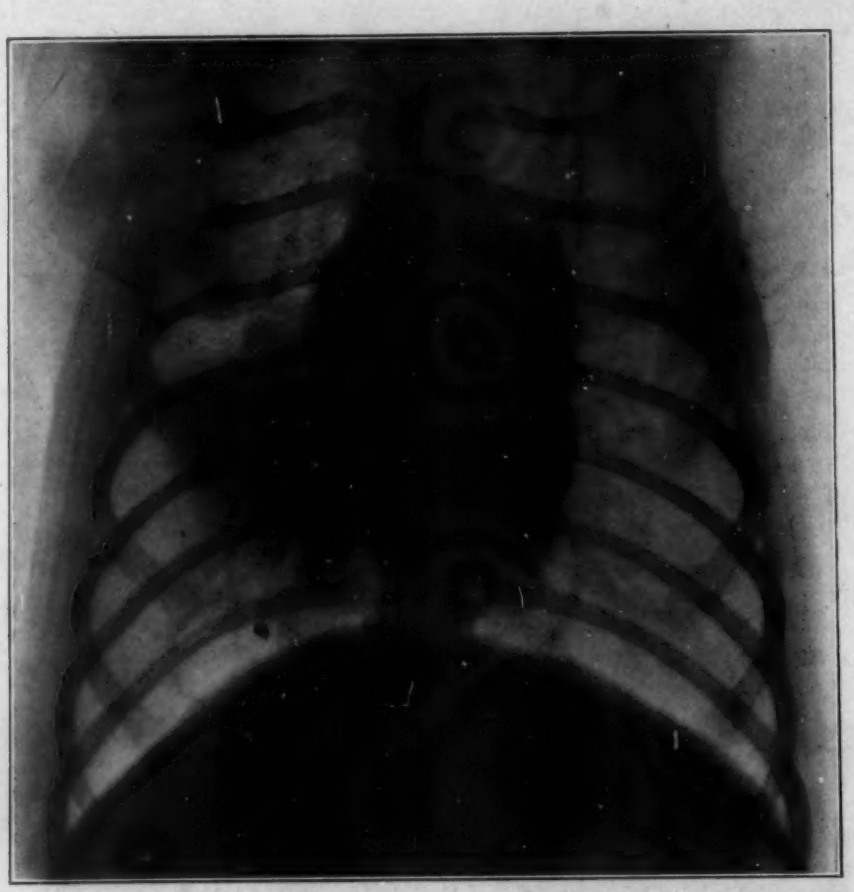


Fig. 6.—Dog Y 36, experiment 17, nineteen days after an infected embolus had been released into the jugular vein; the bit of lead contained in the embolus indicates the position of the thin walled abscess cavity in the right lower lobe; the area of density in the region of the right middle lobe shows the degree of lung consolidation, the result of a complicating distemper. The right middle and lower lobes were removed the following day.

November 25, the dog appeared quite ill. A purulent, hemorrhagic discharge exuded from the nostrils. There was an occasional cough.

November 30, the dog appeared to be improving steadily. The nasal discharge was less in amount, the cough was less severe, and more food was eaten. The external wound had healed by first intention.

December 6, the animal was found dead in his cage. The symptoms had gradually become more pronounced. At necropsy a hemorrhagic, purulent exudate was present throughout the bronchial tree. There was a small amount of clear hemorrhagic fluid in both pleural cavities. There were no pleural adhesions. The bronchial stumps were well healed. The remaining lobes of the lung had the characteristic distemper appearance.

In four dogs one entire lung was removed according to the invagination method by treating each respective lobe bronchus separately. Three

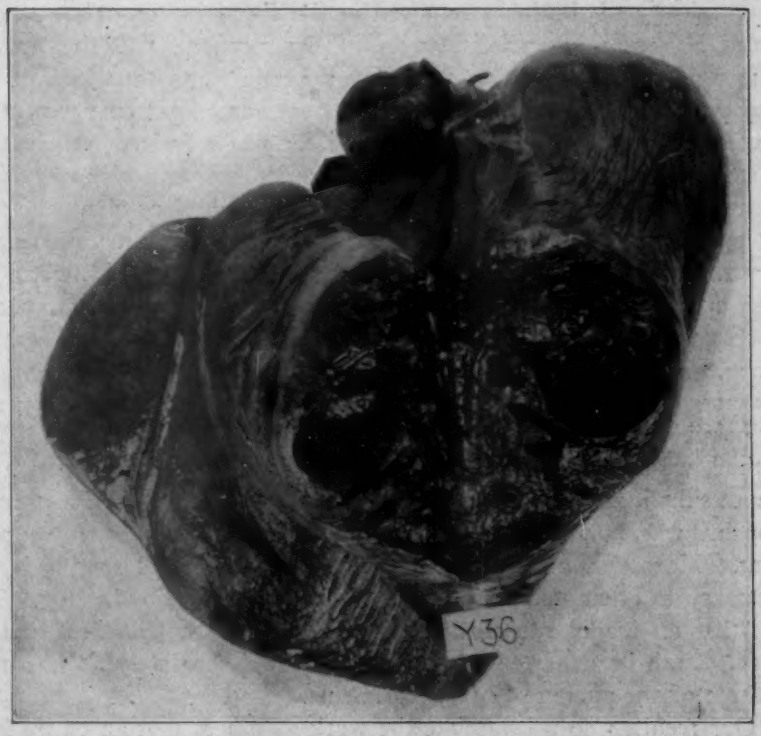


Fig. 7.—The right lower lobe of Dog Y 36, experiment 17, removed at operation; a section taken through the specimen shows the contained abscess cavity.

dogs (experiment 25, dog Y 50; experiment 26, dog Y 53, and experiment 28, dog Y 60) are still living. Dog Y 50 had an abscess in the right lower lobe. The lung removed from dog Y 53 contained no lesion. Dog Y 60 had an abscess in the right middle lobe. One dog (experiment 27, dog Y 59) in which the left lung was removed died on the fourth postoperative day. The lower lobe contained a large abscess and many pleural adhesions were present at the time of the operation. The pleural membranes were markedly inflamed, and it was thought that the dog would probably not survive the operation. We were forced to close the pleural cavity because of the inadvisability of

external drainage which in a dog would certainly produce a fatal pneumothorax. We were not surprised, therefore, to find a well developed empyema at necropsy. The bronchial stump had remained closed. In this particular experiment invagination of the left primary bronchus was done.

CONCLUSIONS

It is evident that direct comparisons cannot be drawn between these experimental results and the results obtained by other investigators. The majority of the lobes removed in the foregoing experiments contained abscesses in various stages of development, and the possible danger of pleural infection following operation was therefore greatly increased. Realization of this handicap necessitated extreme care in the removal of such a lobe and because of the many failures others have experienced in removing one lobe or an entire lung in which our added complication was not present, we felt somewhat dubious about the final outcome. In the first experiments, therefore, we were content in removing only the abscessed lobe. However, our results with lobectomy were encouraging, and the successful removal of a lobe containing an abscess we attribute to the avoidance of infection from the bronchial lumen. A method was devised which would recognize and eliminate this possible source of infection and which would simulate as nearly as possible the technic employed in an appendix operation. This method, we believe, can be applied to any sized bronchus, although we cannot submit sufficient experimental proof. Invagination of a primary bronchus was, however, easily accomplished in one pneumectomy experiment. Moreover, our experiences have led us to feel that it is not necessary to attempt closure of a primary bronchus in the dog. The risk that an inadequate closure of this structure entails need not be taken. Each bronchus to a lobe can be treated separately as was done in three of the pneumectomy experiments.

Our results also substantiate the work of others that an entire lung can easily be removed from dogs, that the animals survive the operation, that they remain free of any deleterious sequelae, and that the severed bronchus heals by scar tissue formation providing infection has not been introduced.

Clinically, the removal of a lobe of a lung would seem to be a less hazardous procedure if infection from the bronchial lumen were avoided. The method devised in this experimental work may be of some assistance in securing an aseptic air-tight closure of a bronchus in clinical cases.

ABSCESSES AND INFLAMMATORY TUMORS IN THE SPINAL EPIDURAL SPACE (SO-CALLED PACHYMENINGITIS EXTERNA) *

WALTER E. DANDY, M.D.
BALTIMORE

Two recent cases of inflammatory tumors in the spinal epidural space presented a picture then unknown to us from a series of spinal cord tumors. In one of the cases the lesion, a tubercle, developed so rapidly as to suggest an extradural abscess; the other, of several months' duration, was looked on as a tumor, despite the high cell count, until the presumed level of the growth was carefully marked out preparatory to operation. When the predicted level of the tumor was found to be identical with an old scar over the spine of a dorsal vertebra, the diagnosis of some inflammatory lesion affecting the cord, though of ill-defined character, appeared to be a probability. When the history had been taken, the patient expressed the belief that his trouble dated from a severe carbuncle of which this directing scar was the result. About the same time my associate, Dr. Frank Ford, recalled an almost identical case, an inflammatory extradural mass, the symptoms of which followed closely on a carbuncle of the back and continued to increase long after its healing. Curiously, these three inflammatory tumors were situated at almost the same cord level and all were confined to the dorsal side of the spinal canal. These facts seemed to suggest not isolated and bizarre spinal infections but rather examples of a well defined type and doubtless also dependent on an anatomic background.

A search of the literature revealed not only a few additional inflammatory extradural masses but also a greater number of acute purulent infections in the epidural space. Strangely enough most, but not all, of these were confined to the same thoracic level and in each the infection was restricted to the dorsal half of the epidural space. There was, moreover, another fact that defined these primary infections as of a special type; namely, similar extradural infections apparently do not develop in the cranial chamber. These infections, therefore, whether acute or chronic, seemed to occur (1) only in the *spinal* epidural space, (2) only in the dorsal half of the spinal canal, and (3) principally in the thoracic region.

An explanation of these findings was sought in the anatomy of the spinal epidural space. However, the current textbooks of anatomy were of little assistance for in none did the epidural space receive more than

* From the Department of Surgery, the Johns Hopkins University Medical Department and Hospital.

brief mention. Dissection of a cadaver shows that the spinal extradural space is present only dorsal to the spinal nerve attachments. Ventral to the nerves the dura is everywhere closely applied to the bones of the vertebrae and their ligaments from the first cervical to the second sacral vertebra. Below the second sacral bony segment the epidural space surrounds the dura on all sides. The epidural space is filled with fat and loose areolar tissue containing numerous veins.

Of greatest importance are the variations in the size of the epidural space. In the cervical region the space is only potential, there being only a few strands of fibrous tissue and almost no fat between the laminae and dura. The epidural space really begins to appear at the seventh cervical vertebra and gradually deepens along the thoracic vertebrae, attaining a depth of about 0.5 to 0.75 cm. between the fourth and eighth dorsal vertebrae. The space tapers again and becomes shallow between the eleventh thoracic and second lumbar vertebrae. Over the remaining lumbar and the first and second sacral vertebrae the epidural space attains its greatest depth. At the second sacral vertebra the dural envelop ends and a continuation of the epidural tissue fills the caudal end of the sacral canal. Only at the lower terminus of the spinal dura does the extradural space extend ventrally; here for a short distance the dura is encircled by the epidural fat and areolar tissue. The size and shape of the epidural space, therefore, appear to be secondary to the variations in size of the spinal cord. Absent over the cervical enlargement and nearly so over the lumbar swelling the epidural space becomes deepest where the spinal cord or the mass of its roots is smallest, i. e., in the upper dorsal and lower lumbar sections. And the space exists only on the dorsal aspect of the dura.

The spinal epidural space is therefore filled with tissues—fat and loose areolar—which offer a foothold for current hematogenous infections, and the intraspinous location of these tissues makes trauma an important inciting agent in the development of hematogenous infections.

Whether the epidural fat performed any normal function other than serving as a padding can hardly be answered unequivocally. It is easy to believe that it acts as a buffer to trauma but such a protective function would appear to be particularly called for in the cervical region, and here the fat is absent. Nevertheless, it would seem to serve some buffer function to direct traumatic insults in the rigid thoracic region. Under certain pathologic conditions the epidural fat is of no little diagnostic and therapeutic value. Practically all spinal cord tumors cause this bed of fat to be absorbed by continuous pressure; in this way the pressure of the tumor on the cord is withheld for a time to a degree commensurate with the volume of the fatty tissue that is destroyed.

During operations for spinal cord tumors the presence or absence of epidural fat, in the thoracic and lumbar but not in the cervical canal,

is carefully noted and considered a sign of great value. If fat is present a tumor beneath the dura is unlikely though not impossible, whereas the absence of fat indicates pressure absorption and, therefore, an underlying neoplasm. The recent work of Peters [1] should be mentioned in this connection. He has shown a frequent involvement of the epidural tissues from primary infections of the spinal meninges. We have, however, found no other reports of persisting epidural infections after cures in any form of meningitis.

We are not concerned in this article with the most common extensions of tuberculous infections from the bodies of the vertebrae into the spinal canal. Such infections are easily recognized by the characteristic picture of vertebral destruction in association with the evidences of spinal compression. Moreover, the epidural space is involved in these cases only because it lies in the path of further extension of the tuberculous process and not because of any peculiar characteristic of the space or its contents. Furthermore, in paraplegia associated with Pott's disease surgery is contraindicated; at least up to this time the results obtained by laminectomy have not been helpful and have usually done harm.

Nor shall we consider here those remarkable chronic inflammatory hypertrophies of the cervical region described by Charcot and Joffroy as pachymeningitis cervicalis hypertrophica, nor the more extensive dural hypertrophies, involving the entire length of the spinal dura, described by Mills and Spiller.[2] These proliferations of fibrous tissue, gradually increasing the bulk of the dura on its inner side, grow into and slowly strangle the spinal cord, causing symptoms that are said to resemble syringomyelia. These rare diffuse increments probably arise from the dura; their origin is considered to be syphilitic. Weinberg [3] has only recently described a localized mass of fibrous tissue arising from the inner side of the dura and compressing the cord. Although he makes a probable diagnosis of tuberculosis from the histologic picture of giant cells, the Wassermann reaction in the spinal fluid was positive. It would, therefore, appear justifiable to question whether the lesion might not have been a gumma, the more common primary dural affection.

ACUTE INFECTIONS IN THE EPIDURAL SPACE (1)

Abscesses of the epidural space arise in two ways: (1) by direct extension of a contiguous infection, and (2) by metastasis through the blood stream.

---

1. Peters, R.: Ueber die Entzündung der Extraduralen Gewebes des Rückenmarks bei der Genickstarre, Deutsche med. Wchnschr. **32**:1151, 1906.

2. Mills, C. K., and Spiller, W. G.: Case of External Pachymeningitis, Implicating the Entire Ventral Surface of the Spinal Dura, Brain **25**:318, 1902.

3. Weinberg, M. H.: Spinal Cord Tumors; Six Cases Including Tuberculosis of Dura, J. Nerv. & Ment. Dis. **63**:23 (Jan.) 1926.

Albers, 1833, from Germany has been credited with first reporting an acute infection of the epidural space. Ducheck, 1853, gave to this condition the name peripachymeningitis, which was later changed to pachymeningitis externa. Cases have been reported under both titles. As will be shown later, both appellations are misnomers for the infections are not of the meninges as was then supposed but of the tissues of the epidural space.

As we have had no patient in whom an abscess of the extradural space has either been suspected during life or found at necropsy we can only assemble and analyze the cases from the literature. Doubtless those which have been compiled are only a small fraction of the actual number of either the acute or chronic infections, for many have received but casual mention or are hidden in obscure or inaccessible publications. Though infections of the epidural space are comparatively rare it is worthy of note that Morowitz [4] had three acute hematogenous abscesses in one year and we had two cases of chronic infection in a somewhat shorter period.

The best bibliography on this subject has been assembled by R. Kaminski (Eine Metastatische Peripachymeningitis und Periostitis spinalis purulenta nach Furunkulose, inaugural dissertation, Greifswald, 1917). Through him we learn that Hasse (three cases) and Ducheck, 1853, have described extradural abscesses secondary to direct extension of an infection from decubitus; Traube, 1863, a case from a psoas abscess and another from an extrapleural abscess. In Mannkopff's case the epidural abscess was an extension of Ludwig's angina. Recently Taylor and Kennedy,[5] 1923, reported an extrathecal lumbar abscess (*Staphylococcus aureus*) which was an extension of an acute pericostal inflammation.

The most interesting extradural infections, and those which present a much more difficult problem in diagnosis, are of hematogenous origin. Quite a series of these has been assembled. In many the infection has been identified as a metastasis from an infection elsewhere in the body, i. e., staphylococcus phlebitis,[6] furunculosis,[7] furunculosis leg [4] (also by Kaminski), furunculosis neck [8] and diplococcus bronchitis.[9]

---

4. Morowitz, P.: Ueber akute eitrige Perimeningitis (Peripachymeningitis), Arch. f. klin. Med. **128**:294, 1919.

5. Taylor and Kennedy: A Case of Extrathecal Abscess of the Spinal Cord, Arch. Neurol. & Psychiat. **9**:652 (May) 1923.

6. Oppenheim, E. S.: Ueber einen Fall von extraduraler spinal Eiterung, Berl. klin. Wchnschr., 1910.

7. Cassirer: Die Pachymeningitis externa purulenta, Oppenheim's Lehrbuch der Nervenkrankheiten, Ed. 7, **1**:419, 1923.

8. Hoestermann: Ueber myelitis transversa, Neurol. Centralbl., 1913.

9. Schick, K.: Pachymeningitis spinalis externa purulenta als Metastase nach Diplokokkenbronchitis, Wien. klin. Wchnschr. **22**:1185, 1909.

In three cases, of Lewitzky,[10] Spencer,[11] and Hinz,[12] necropsy revealed no other infection in the body; the abscesses were therefore assumed to be primary in the epidural space. Although Hinz assumed the infection to have probably arisen from a puerperal thrombosis, the extrathecal infection appeared four weeks after a normal pregnancy, the first symptom of the fatal illness being uterine bleeding; no evidence of uterine infection was found at necropsy. Trauma appears to have been an inciting agent in the case of Kaminski and, according to Cassirer, in cases reported by Runge and Pulvirenti.

A study of the accompanying table of acute epidural infections discloses several striking facts. There have been only two recoveries in the entire series of twenty-five cases (Pulvirenti, Taylor and Kennedy[5]): both of these followed drainage of the infection. Apparently in only the four cases subjected to operation was a diagnosis even suspected before the necropsy findings, and except in Taylor and Kennedy's case there is no evidence to indicate that the nature of the lesion was more than roughly guessed. Without exception the acute infections have been fulminating, death usually resulting in two or three weeks; the minimum duration of life is six days and the maximum thirty days.

How effective operative treatment will be for abscesses of this character can, of course, only be conjectured. Much will necessarily depend on the virulence of the organism, the resistance of the patient and the extent of the infection in the epidural space. Tightly sealed within the vertebral canal, an abscess can hardly rupture into the soft tissues and be spontaneously cured. The only possible avenue of escape would be through an operative defect in the laminae.

At first glance it might appear that the structure of the epidural space would preclude any practical operative drainage. From the high cervical region to the sacral canal the epidural space is continuous, i. e., it is not intercepted by mechanical barriers. But relatively poor as fatty tissue is known to be in combating infections, it is actually able to build a barrier of inflammatory tissue and restrict the acute infection to a small fraction of the epidural space. It is not improbable, in fact it seems more reasonable to believe, that the resistance to infections in the epidural space is largely due to the vascular areolar tissue and not to the fat. In only two (Kaminski, Spencer[11]) of ten cases in which the location of the abscess has been mentioned has the infection spread

10. Lewitzky, P.: Ein Fall von Peripachymeningitis spinalis, Berl. klin. Wchnschr. **14**:227, 1877.

11. Spencer, N. H.: Case of Idiopathic Inflammation of the Spinal Dura Mater, Lancet, June 14, 1879, p. 836.

12. Hinz, R.: Ueber einen Fall von Perimeningitis purulenta, Deutsche med. Wchnschr. **47**:1229 (Oct. 13) 1921.

I. Acute Infections (Abscesses),

Reported by	Age and Sex*	Secondary to	Primary Origin	Incited by Trauma	Location of Infection	Symptoms of Onset	Pain; Location	Character of Pain	Paraplegia	Paralysis: Time of Onset; Time Until Complete	Bladder or Rectum
Oppenheim[6] 1910	40 ♀	Phlebitis (staphylococcus)	Metastatic	..	VI dorsal to I lumbar	Sudden pain	+ Lower thoracic vertebrae and legs	Increasing until terrific	+	6th day; rapid increase	.....
Hinz[12] 1921	29 ♀	.....	Primary (?)	..	IV to VIII dorsal	Backache	+ Back	Backache	+ Flaccid	4th day; sudden	Retention
Morowitz[4] 1919	15 ♀	Healed furunculosis of leg	Metastatic	..	Lower thoracic	Sudden terrific pain	+ Inguinal region bilateral	Spread next day to back and abdomen	+	9th day; 1 day	.....
Morowitz[4] 1919	26 ♂	.....	Metastatic	..	Lower thoracic	Sudden severe pain	+ Back and legs	Severe, continuous	None	None; none	.....
Morowitz[4] 1919	15 ♀	.....	Metastatic	..	.....	Dizziness and chill	+	Headache	..	.....	.....
Cassirer[7] 1923	..	Furuncle	Metastatic	..	.....	.....	.....	.....	+	.....	.....
Spencer[11] 1879	..	.....	Primary	+	Whole canal	.....	.....	.....	..	.....	.....
Lewitzky[10] 1877	..	.....	.....	..	.....	.....	.....	.....	..	.....	.....
Lemoine and Lannois[19] 1882	..	.....	.....	..	.....	.....	.....	.....	..	.....	.....
Mollière[20] 1897	..	.....	.....	..	.....	.....	.....	.....	..	.....	.....
Hoestermann[3] 1913	..	Furuncle of neck	Metastatic	..	V to VII dorsal	.....	.....	.....	..	.....	.....
Kaminiski 1917	15 ♀	Furunculosis of leg	Metastatic	..	Whole length	Sudden pain	+ Knees; then inguinal and finally in back	Terrific	+ Below dorsal II	9th day; sudden	Retention
Schick[9] 1909	40 ♂	Bronchitis (diplococcus)	Metastatic	No	Lower cervical and upper thoracic	Sudden pain in both arms	+ Both arms, shoulder and upper vertebrae	Very severe	+ Weakness of arms later	9th day; sudden	Retention
Traube, 1863, cited by Kaminiski	..	.....	Metastatic	..	.....	.....	.....	.....	..	.....	.....
Albers, 1833, cited by Kaminiski	..	.....	Metastatic	..	.....	.....	.....	.....	..	.....	.....
Pulvirenti, 1921, cited by Cassirer	..	.....	Primary	+	III–IV lumbar	.....	.....	.....	..	.....	.....
Runge, 1920, cited by Cassirer	..	.....	Primary	+	.....	.....	.....	.....	..	.....	.....

I. A. Acute Infections (Abscesses), Resulting from

Taylor and Kennedy[5] 1923	15 ♀	Abscess along ribs	.....	..	Lower thoracic and lumbar	Pain and chills	+ Lower ribs	Severe and sharp	Complete	13th day; 2 days	Retention
Mannkopf, 1864, cited by Kaminiski	..	Ludwig's angina	.....	..	.....	.....	.....	.....	..	.....	.....
Barth, cited by Kaminiski	..	Puncture wound	.....	..	.....	.....	.....	.....	..	.....	.....
Hasse, cited by Kaminiski	..	Decubitis	.....	..	.....	.....	.....	.....	..	.....	.....
Hasse	..	Decubitis	.....	..	.....	.....	.....	.....	..	.....	.....
Hasse	..	Decubitis	.....	..	.....	.....	.....	.....	..	.....	.....
Ducheck, 1853 cited by Kaminiski	..	Decubitis	.....	..	.....	.....	.....	.....	..	.....	.....

* In this table ♂ indicates male. ♀ female.

19. Lemoine, G., and Lannois, M.: Perimeningitis Spinale Aigue, Rev. de méd. **2**: 533, 1882.

20. Mollière, H.: Note sur un cas de Périméningite spinale primitive Suppurée, Lyon méd., 1897, p. 143.

Primary or Metastatic

Sensation	Spine: Rigidity; Tenderness	Kernig Sign	Headache	Leukocytes	Temperature	Reflexes	Spinal Fluid	Duration of Life	Operation	Result	Clinical Diagnosis	Remarks
.....	.....	..	..	....	Fever	.....	....	30 days	None	Death; necropsy	....	Ribs, vertebrae and spinal cord not involved; infection during sixth month of pregnancy
Absent below dorsal VI	+ on 5th day; 5 to 12 dorsal	..	..	....	40 C.	.....	Clear, no sediment	6 days	None	Dead; necropsy	Thrombosis; embolus; puerperal myelitis	Normal pregnancy concluded 1 month before symptoms of onset; uterine bleeding began at time of onset of backache; fever appeared only on third day; organism not determined; cord and vertebrae not involved
Lost	Lower thoracic tender	..	..	18,000	40 C.	.....	....	15 days	None	Dead; necropsy	.....	Walked home after sudden onset of pain; bedfast next day and thereafter
Hyperesthesia	Lower thoracic and upper lumbar tender	+	..	.....	.....	.....	....	10 days	None	Dead; necropsy	.....	Multiple abscesses in lungs and kidneys
Hyperesthesia	Neck rigid	+	+	.....	Fever	.....	....	19 days	None	Dead; necropsy	.....	Many abscesses elsewhere
.....	.....	..	..	.....	.....	.....	....	.....	+	?	?	Abscess found at operation
.....	.....	..	..	.....	.....	.....	....	17 days	None	Dead; necropsy	....	Extradural abscess extending from 3 inches (7.6 cm.) below head to sacrum; no mention of dorsal or ventral position
.....	.....	..	..	.....	.....	.....	....	22 days	.....	Dead; necropsy	Meningitis	
.....	.....	..	..	.....	.....	.....	....	.....	.....	Dead; necropsy	.....	
.....	.....	..	..	.....	.....	.....	....	.....	.....	Dead; necropsy	.....	
.....	.....	..	..	.....	.....	.....	....	.....	+	Dead; necropsy	.....	
Diminished	.....	..	+ Later	18,000	41 C.	.....	Cocci; leukocytes	10 days	None	Dead; necropsy	.....	Gram-positive staphylococcus organism; thick layer of pus in fatty tissue; cord normal; whole length of canal involved
Absent	+ neck and and thoracic vertebrae	..	..	.....	.....	.....	Diplococci	28 days	.....	Dead; necropsy	.....	Opisthotonus; hiccup continuous for 2 weeks before death
.....	.....	..	..	.....	.....	.....	....	.....	.....	Dead; necropsy	.....	
.....	.....	..	..	.....	.....	.....	....	.....	.....	Dead; necropsy	.....	
.....	.....	..	..	.....	.....	.....	....	Recovery	+	Recovery	... .	Cassirer says healing after operation
.....	.....	..	..	.....	.....	.....	....	.....	.....	Dead; necropsy	.....	

the Direct Extension of Contiguous Infections

Absent	.....	..	..	18,000	104	.....	....	Recovery	+	Recovery	Extradural abscess	Staphylococcus aureus from culture; patient survived and some function returned
.....	.....	..	..	.....	.....	.....	....	.....	.....	Dead; necropsy	.....	
.....	.....	..	..	.....	.....	.....	....	.....	.....	Dead; necropsy	.....	
.....	.....	..	..	.....	.....	.....	....	.....	.....	Dead; necropsy	.....	
.....	.....	..	..	.....	.....	.....	....	.....	.....	Dead; necropsy	.....	
.....	.....	..	..	.....	.....	.....	....	.....	.....	Dead; necropsy	.....	
.....	.....	..	..	.....	.....	.....	....	.....	.....	Dead; necropsy	.....	

II. Inflammatory Tumors

Reported by	Age and Sex*	Secondary to	Primary Origin	Incited by Trauma	Location of Infection	Symptoms of Onset	Pain; Location	Character of Pain	Paralysis: Paraplegia	Paralysis: Time of Onset; Time Until Complete	Bladder or Rectum
Stroubell[13] 1898	86 ♀	.....	Syphilis (?)	..	III to VI dorsal	Paraplegia and anesthesia	.....	.....	Complete	Sudden	.....
Schultze[16] 1903	24 ♂	.....	Chronic inflammatory tissue	..	V to VII dorsal	Pain	+ Lower ribs and back	Sudden, excruciating	Partial, spastic	3 months; 6 months	Disturbed function but no retention
Fischer[21] 1902	44 ♂	.....	Syphilis (?)	..	III to VI dorsal	Pain in vertebrae and legs	+	.....	+	.....	Retention and incontinence
Mendel[17] 1909	..	.....	Chronic inflammatory tissue	..	V to IX dorsal	Pain in head, neck and back	+ Head, neck and back	Severe	Partial	2½ years; partial	.....
Pelz[22] 1917	67 ♂	.....	Tuberculosis	..	Middle and lower thoracic	Pain in back	+ Back and later legs	.....	Total	4½ months	Incontinence (last 2 weeks)
Gampers 1920	..	.....	Tuberculosis	..	Lumbar	.....	.....	.....	..	.....	.....
Lewis and Bassoe 1915	21 ♀	.....	.....	No	V and VI dorsal	Numbness and pain in legs	Toes	Cramp	Complete	3 weeks	Slight hesitancy in voiding
Dandy 1926	42 ♂	Direct extension from furuncle on back	Chronic inflammatory tissue	No	V to VIII dorsal	Pain	+ Back and sides	Severe, sharp	Partial	10 months; partial	Incontinence
Dandy 1926 (Dr. Ford's case)	Middle age ♂	Direct extension from furuncle on back	Chronic inflammatory tissue	No	V to VIII dorsal	Pain	+ Back and waist	Severe, sharp	Partial	3 months; partial	Incontinence
Dandy 1926	27 ♀ (colored)	.....	Tuberculosis	+	III to VI dorsal	Pain	+ Back and sides	Very severe	Complete	8 months; 3 days	Incontinence, then retention

* In this table ♂ indicates male, ♀ female.

21. Fischer: Ein Fall von Pachymeningitis chronica externa spinalis, Verhandl. d. Gesellsch. deutsch. Naturf. u. Karlsbad **2**: 16, 1902.

22. Pelz, A.: Kasuistische Beiträge zur Lehre von den Rückenmarks Geschwülsten, Arch. f. Psychiat. **58**: 195, 1917.

(No Abscess)—Continued

Sensation	Spine: Rigidity; Tenderness	Kernig Sign	Headache	Leukocytes	Temperature	Reflexes	Spinal Fluid	Duration of Life	Operation	Result	Clinical Diagnosis	Remarks
Absent	.....	..	..	.....	.....	Absent	....	.....	.....	Dead; necropsy	.....	Reflexes absent; no clonus; granulation tissue tumor, not like tuberculosis—probably syphilis
Sensory level gradually became higher	None: V to VI dorsal	..	..	.....	.....	Increased ankle clonus	....	10 mos.	+	Dead; necropsy	.....	After 5 weeks the pain improved but quickly became worse when numbness of feet ensued; persisted 7 months, then again disappeared but returned for an hour every time he bent over; pain worse on coughing and sneezing; ankle clonus; died of meningitis after operation; tumor dorsal side of dura; grayish red solid mass 12 cm. long, 1 cm. thick; connective tissue strands and cluster of cells
Absent	.....	..	..	.....	.....	Increased clonus	....	1 yr.	No	Dead; necropsy	.....	Mass of fibrinous tissue containing giant cells; thinks it histologically more like syphilis; no evidence of tuberculosis
Partial loss	.....	..	..	.....	.....	.....	....	3 yrs.	+	Dead; necropsy	.....	Tumor 9.6 cm. long; granulation tissue without specific character; no necrosis or giant cells
.....	.....	..	..	.....	.....	.....	....	16 mos.	No	Dead; necropsy	.....	Pain in legs developed only after 4 months; weakness came soon after; tumor 1 cm. long, 1 cm. thick; all on outer side of dura; granulation tissue with many giant cells and tubercles
.....	.....	..	..	.....	.....	.....	....	.....	.....	Dead; necropsy	.....	No involvement of vertebrae
Absent	Very little	..	..	.....	.....	.....	Normal	Well	Spinal decompression	Well	Tuberculous involvement of cord	Patient was in seventh month of pregnancy when symptoms began; was allowed to go to term and labor was successfully completed; 3 weeks later decompressive laminectomy; indurated mass of fat in epidural space (dura not opened); quick return of function; complete restoration of motor power in 3 years
Sensory level	+; +	+	No	.....	No	Greatly increased Babinski reflex +	53 cells; xanthochromia	Well	+	Well	Inflammatory tumor	Pain in back and sides persisted 6 months; since then somewhat diminished; convulsions in legs 1 month; diagnosis of an inflammatory tumor was made before operation; return of function
Sensory level	+; +	..	..	.....	No	Greatly increased Babinski reflex +	9 cells; lymphocytes	Well	+	Well	Tumor	This case is presented by permission of Dr. Ford; the operation was performed in Bellevue Hospital, New York; a firm fibrous mass 6 cm. long and 1 cm. thick removed; return of function
Total absence below sensory level	+; +	..	..	.....	.....	.....	15 cells; lymphocytes	Well	+	Well	Tuberculosis of spine and abscess	Struck back 8 months before; pain had persisted since in that spot; any movement intensified pain; return of function; Wassermann reaction from blood and spinal fluid negative; no tubercles seen

throughout the length of the epidural space. In such instances operative efforts would necessarily be fruitless. In those cases in which the infection has been walled off, there is every reason to believe drainage would result in a cure.

Doubtless operative results will always be dependent on the stage at which the diagnosis is made. It would appear probable that an abscess though at first walled off must, when increasing rapidly and becoming tense, break its plastic barriers and spread up and down the epidural space. An early diagnosis followed by operation may well prevent diffusion and facilitate restriction of the infection. It is fortunate at least that the epidural space and its infections are located on the dorsal side of the spinal dura. Were the abscesses situated ventrally drainage would be extremely difficult if not impossible.

There should be little if any difficulty in arriving at a diagnosis of an epidural abscess when the signs of spinal cord compression (accompanied by fever and leukocytosis) develop and the level of the spinal cord injury is contiguous to a preexisting infection. Nor would it appear that the diagnosis of hematogenous abscesses of the epidural space would offer insuperable obstacles. In fact the signs and symptoms of this group (I) seem to be sufficient distinctly to suggest a clinical entity. In practically all of these cases the symptoms of onset is a terrific, almost unbearable and unrelenting pain (1) in the back, or (2) along the course of the spinal nerves (bilateral), or (3) in the legs. In a previous article these types of pain have been attributed, when caused by spinal cord tumors, to involvement of (1) the vertebrae, (2) the spinal nerves, and (3) the sensory paths in the spinal cord. But these pains are much more severe and persistent in inflammations than when due solely to pressure from a tumor. The pain in spinal tumors, or in fact in any other proved lesion, though seemingly of the same kind, cannot approach in severity or persistence the pains of infection of the epidural space.

The next most impressive evidence of abscesses of the epidural space is the latent period of a few days (from four to nine) between the time of onset of the excruciating pain and motor, sensory and sphincter paralysis.. In every instance paraplegia, as well as sensory and sphincter loss, has either been sudden or has become complete within forty-eight hours after its onset. In nearly all cases there has been a sharp bilateral sensory level which may or may not have ascended, doubtless depending on whether the epidural abscess has extended upward or has remained localized. In addition to this characteristic story there is always high fever, tachycardia, leukocytosis (18,000 in three cases) and probably always tenderness and rigidity of the spine. Although there are few records of examinations of the spinal fluid (in two cases organisms were grown in cultures of the cerebrospinal fluid, possibly because the

needle passed through the epidural infection) there must always be an increased cell count (polymorphonuclear cells) as the reaction to an adjacent acute infection. Manometric tests have also not been made in these cases but since the paralyses are evidence of spinal cord compression, a complete block of the spinal canal must surely exist. Such a block was demonstrated in both of our inflammatory tumor cases, in one of which the symptoms of spinal cord involvement developed almost as suddenly as in any of the acute abscesses. Whether an acute epidural abscess may eventually be diagnosed before implication of the spinal cord and before the appearance of a spinal block remains to be seen. At least a pain that appears so distinctive should put us on guard for the earliest sensory or motor changes. Experience has taught us that the more rapidly spinal compression causes paraplegia the more slowly recovery takes place after its relief. Gradual compression of the spinal cord allows a remarkable adjustment to the tumor's bulk; often the spinal cord may be reduced to half its cross sectional volume with little or no loss of function, but after the removal of a slowly growing tumor the recovery of function is very rapid.

The sudden onset of paraplegia in these cases has led to the diagnosis of myelitis or even of thrombosis or embolism. All these conditions should be eliminated by the excruciating pain which for several days precedes paralysis, by the tenderness and rigidity of the spine and by the demonstration of a spinal subarachnoid block. Although meningitis might appear possible because of rigid neck, a positive Kernig's sign, fever and leukocytosis, the sensory and motor level and the cerebrospinal fluid examination, together with the absence of a spinal subarachnoid block, should easily exclude this diagnosis. The possibility of an abscess of the spinal cord might also be considered but the interval of pain that precedes paraplegia in epidural abscesses would doubtless be absent.

INFLAMMATORY EPIDURAL TUMORS (II)

The story in this group of cases is very different. While the pain is of the same general character and extremely severe, it lacks the very sharp onset; it is less fulminating and is prolonged over a period of weeks or months instead of days. The latent period preceding paralysis is far longer and the paralysis is usually slow in developing and usually incomplete. In brief all manifestations are chronic instead of acute. In only two cases (Stroubell,[13] Dandy [14]) did the symptoms of spinal cord compression appear suddenly, and only in these instances and a case

13. Stroubell: Ueber Syphilis der Rückenmarkshäute, Neurol. Centralbl., 1898, p. 1120.

14. Dandy, W. E.: The Diagnosis and Localization of Spinal Cord Tumors, Ann. Surg. **81**:223 (Jan.) 1925.

of Lewis and Bassoe [15] was the paraplegia complete. In the remaining cases the motor, sensory and sphincter changes developed so slowly (from three months to two and one-half years) as to suggest tumors rather than infections. Four of these tumors have been described as syphilitic or tuberculous because of the histologic demonstration of giant cells and occasional tubercles. Since the histologic differential diagnosis between syphilis and tuberculosis is so often impossible, it is not safe to assume that all of these cases are due either to syphilis or tuberculosis. In our patient syphilis was excluded by the negative Wassermann reaction in both the blood and the spinal fluid. Tuberculosis seemed more probable because of her race (colored), but tubercles could not be definitely demonstrated in sections of the tumor nor was there any other evidence of tuberculosis in the body. She has, moreover, remained well and free of any symptoms or signs of tuberculosis since the operation, over two years ago. In her case trauma seemed to play a definite inciting rôle; at least she refused to yield from her original story that a pain developed immediately after a blow on the spine and that it persisted in the same spot. And precisely at that spot the tumor was found at operation. A remarkable feature of this case is that an inflammatory tumor probably existed eight months (its gross appearance also supports the slow growth of the tumor) before any symptoms of paralysis and then paraplegia became complete in three days, and without abscess formation.

Four cases of this group would appear to be of staphylococcus origin, those of Schultze,[16] Mendel [17] and Dandy [14] (two). In our two cases the organisms were identified by cultures. In the cases of Schultze and Mendel the infections were probably of metastatic origin. In our two cases the epidural infections were undoubtedly due to the direct extension of the outskirts of deep middorsal carbuncles. These two cases strikingly demonstrate how differently infections are handled by different tissues. In both of our cases the original carbuncle in the soft tissues of the back had long since healed (five and thirteen months) leaving only a scar, whereas at the end of this time the areolar and fatty tissues of the epidural space were still struggling to wall off the same organisms, which could not be destroyed. In slowly subduing these infections the newly formed inflammatory tissues assumed the proportions of tumors. That living organisms were still present in the connective tissue masses was demonstrated by bacterial stains of the sections,

15. Lewis, Dean; and Bassoe, P.: Frazier's Surgery of the Spine and Spinal Cord, 1918, p. 922; Surg. Gynec. Obst. **20**:489, 1915.

16. Schultze, F.: Zur Diagnostik und Operativen Behandlung der Rückenmarks hautgeschwülste, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **12**:153, 1903.

17. Mendel, K.: Meningo myelitis unter der Bilde eines Rückenmarkstumors, Berl. klin. Wchnschr. **46**:2239, 1909.

by the presence of minute abscesses in the connective tissue and in one case by the growth of *Staphylococcus aureus* from cultures of the tumor at operation. Moreover, in both these cases the infection was again lighted up by the trauma incident to the operation; the wounds promptly broke down and from one wound *Staphylococcus aureus* was grown in culture.

In all these chronic inflammatory tumors (except in Lewis' case) pain in the back, though far less excruciating than in the epidural abscesses, has been much more severe than from neoplasms whether of intradural or extradural origin. The cell count from the cerebrospinal fluid in our three cases was 9 (tubercle), 15 and 53—all lymphocytes.

The age of the patients afflicted with inflammatory tumors averages higher than of those with abscesses. The series of cases is, however, too limited to warrant conclusions on this point. It is also worthy of note that with one exception [18] these inflammatory tumors have been in the thoracic epidural space and nearly all between the third and ninth vertebrae. Again the series is too small to allow us to consider this too significant. Two facts, however, are suggested as a possible explanation of this greater incidence in the thoracic region: (1) carbuncles and furuncles are more common in the thoracic than the lumbar region; (2) spinous processes are more superficial in the thoracic region and therefore the spine is protected by less soft tissues and is also more susceptible to trauma.

All the tumors have been well formed and firm. In one of our cases it was of cartilaginous consistency and so tightly bound to the dura that considerable force and sharp dissection with a periosteal elevator was necessary to strip it from the dura. The masses of inflammatory tissue averaged about 1 cm. in depth; the longest was 12 cm. One of ours weighed 15 Gm.

In our three cases the tumor was removed. An equally good result, however, was obtained by Lewis [15] by a simple decompression laminectomy. It is interesting that in his patient operation was delayed over two months to allow the completion of a full term pregnancy. It is also worthy of note that pain was not a conspicuous feature in the case—the sole exception—through the involvement of the fat with inflammatory tissue seemed similar to the other cases in this group.

REPORT OF THREE CASES OF CHRONIC INFLAMMATORY TUMORS OF THE EPIDURAL SPACE

CASE 1.—A large, well nourished man, aged 42, was referred by Dr. L. F. Barker because of gradually progressive paraplegia and anesthesia, suggestive of a spinal cord tumor. The patient persisted in dating his illness from a carbuncle and a series of boils in the back thirteen months before. During

18. Gampers, E.: Beitrag zur Pathologie und Therapie der Erkrankungen der Cauda Equina, Jahrb. f. Psychiat. u. Neurol., 1920, p. 40.

this illness he suffered severe pains in the back and sides and after healing of the infection the character and the intensity of these pains persisted. For the following six months the pains steadily increased; all efforts to allay them were futile. Since then the pains in the sides has been present only at times but the terrible backache had remained practically unchanged.

Three months previously numbness appeared almost synchronously in both legs. Two weeks later the patient's gait became affected and it was soon necessary to use a cane in walking. Loss of equilibrium and of motor power progressed gradually. One month later both legs became spastic and involuntary jerkings (he aptly termed them "convulsions") appeared. The spastic contractions became so powerful that it was often impossible voluntarily to counteract the muscular pull. At times the legs would be fixed in the extended position and again strongly flexed at the hips and knees. The contractions were very painful. The numbness seemed gradually to extend up the legs and abdomen and finally settled at a level above the umbilicus. Girdle pains and a feeling of constriction developed and persisted in this region. Sneezing produced a queer tingling in his feet.

On admission he was able to walk a few yards with great effort and only when supported, but as attempts at walking brought on the painful clonic contractions he was reluctant to stand. All motor and sensory functions in the upper extremities were normal.

Dr. Barker's examination showed in addition to the motor loss a sharp girdle of hyperesthesia at the eighth thoracic segment with marked loss of sensation to pain, touch and temperature below this level; almost complete loss of muscle sense in both feet; greatly exaggerated knee kicks and Achilles reflexes; a bilateral positive Babinski reflex and ankle clonus. The epigastric reflexes were obtainable but the abdominal and cremasteric reflexes were absent. There had been no incontinence of urine or feces. Examination of the spinal fluid showed xanthochromia, heavy globulin and fifty-three lymphocytes.

It was Dr. Barker's opinion, in which I concurred, that the patient's condition was due to a spinal cord tumor, the localization of which was quite accurately determined by the sharp girdle of altered sensation. We were disturbed by the high cell count and heavy globulin, neither of which could be satisfactorily explained.

Despite the patient's persistence in associating his symptoms with the series of boils on his back thirteen months before, there seemed to us little possibility of lesion from this source at this late date. However, when according to custom the presumed site of the tumor was scratched by a scalpel for operative localization the marker bisected a round scar over the sixth thoracic spine, obviously the scar of an old carbuncle. The association of the scar and the marker for orientation was too striking to disregard as a coincidence. At once it seemed that there must be some relationship between the old inflammatory process and his tumor. Accordingly I dropped out of the operation to convey this impression to Dr. Barker but both of us felt that the lesion was such as to require exploration.

At operation when the laminae of the sixth and seventh vertebrae were removed a reddish brown mass at once appeared in lieu of the normal extradural fat. The tumor was so fibrous and lacking in cellular elements that an extradural sarcoma, the only likely form of tumor in this location, appeared inconceivable. It was thought to be an inflammatory mass. Frozen sections verified this diagnosis. To get above and below this growth it was necessary to remove extra laminae, the fifth and eighth, i. e., the laminae of four vertebrae in all.

Epidural fat was then encountered both above and below the tumor mass and dissection was begun from below upward. The mass was so tightly bound to the dura and it so overhung the lateral margins of the dura that dissection in toto made no progress. The tumor was then bisected longitudinally in the midline, which was the deepest part of the mass; it presented on cross section a semilunar shape. Even then blunt dissection of the tumor was impossible. So tightly was the tumor bound to the dura and so hard was the tumor that I believe the spinal dura could have been pulled from its attachment before the mass would have separated or the tumor broken. With a sharp periosteal elevator the mass was cut away from the dura, there being scarcely a suggestion of a line of cleavage. The inflammatory mass after removal measured 11 cm. long, 2 cm. deep, and was as wide as the spinal dura which

Rigid mass of inflammatory tumor removed from the epidural space in case 1; microscopically the tumor was purely inflammatory.

it covered; it weighed 15 Gm. Minute foci of cellular tissue were seen throughout a cut section of the tumor, also little islands of infiltrated fat. There was no evidence of pus. Under the microscope the cellular foci were seen to be miliary subacute abscesses, polymorphonuclear cells predominating. They were surrounded by dense walls of fibrous tissue. Unfortunately cultures of the tissues were not made at operation.

The entire wound quickly broke down from infection. *Staphylococcus aureus* was grown from cultures of the wound, the organisms doubtless liberated from the miliary abscesses of the tumor and stimulated to renewed activity by the operative trauma.

Two months after operation the patient was discharged with the wound healed. Recovery of function, though slow, has been gradual and complete. Two and a half years later he remains perfectly well.

The tumor, therefore, is of inflammatory character. It surely arose from direct extension of the infection of an old carbuncle of the back (thirteen months before operation) into the extradural fat.

CASE 2.—The second patient was a colored woman, aged 27. She was admitted to the medical service of the Johns Hopkins Hospital because of a rapidly progressive paraplegia. Eight months before she fell down three or four steps, striking her back in the upper thoracic region. She spent the day in bed because of pain in her back and side. The pain in the back had persisted without remission, but the pain in the side had disappeared at times, though the longest free interval has not been greater than a week. The pain in the back was dull and aching; that in the chest, sharp and cutting. She had not been able to bend forward, even to look down, because any movement of the back intensified the backache. For the last three weeks the pains in the back and chest had been particularly severe; they "cut off her wind" if she bent her body.

Nine days before operation both legs suddenly gave way so that she could scarcely walk. A loss of sensation developed synchronously and rapidly extended upward until a sharp level was reached at the lower costal margin on both sides. She volunteered that she had since been unable to contract her abdominal muscles.

Seven days before admission she developed incontinence and three days later incontinence gave way to retention, catherization being necessary. There had never been spasticity.

Examination showed total flaccid paralysis of both legs; the upper extremities were unimpaired. A sharp sensory level crossed the thorax just below the xiphoid process; below this line there was complete anesthesia to pain, touch and temperature; there was total loss of muscle sense. The epigastric and abdominal reflexes were absent. The left knee kick was feebly present but the right knee kick and both ankle jerks were absent. There was no response to plantar stimulation. Marked tenderness was elicited on deep pressure about the spine of the fourth, fifth and sixth thoracic vertebrae. The spinal fluid examination made on the medical service showed fifteen cells, all leukocytes.

In Queckenstedt's test the cerebrospinal fluid rose 20 mm. from a base level of 115 mm. following compression of both jugular veins; but the level was not restored on release of the jugular pressure. Several times this was repeated with the same results. Roentgen-ray examination of the spine was negative; the Wassermann reaction from the blood and spinal fluid were negative.

Air injection into the spinal canal showed a sharply defined block in the spinal canal at the fourth thoracic vertebra. Immediately on the introduction of the air into the spinal canal her original pain was duplicated and intensified. The injected air did not reach the cranial chamber.

Because of the great rapidity of the paralysis a tuberculous abscess was suspected, probably in relation to a diseased vertebra, though roentgen-ray examination was negative.

At operation a mass of inflammatory tissue was removed from the extradural space between the third and fifth thoracic vertebrae, inclusive. The mass was firm and sharply defined above, below and laterally. It covered only the dorsal aspect of the spinal dura from which it was completely removed.

Microscopic sections showed chronic inflammatory tissue containing many giant cells. The pathologic diagnosis was tuberculous granuloma.

Return of motor and sensory functions began two weeks after the operation and progressed slowly. She could walk in three months. It is now two years since the operation and the patient has remained perfectly well. Her gait is absolutely normal.

CASE 3.—To the foregoing cases I append a third by permission of my associate, Dr. Frank R. Ford. The patient was an Italian laborer who was under Dr. Ford's care at Bellevue Hospital, New York. He had been admitted because of weakness and stiffness of the legs. Five months before his entry into the hospital he was infected with a series of furuncles over the back. These caused severe pain over the back and around the waist. For several weeks after the furuncles had healed, the pain continued severe and the spine was so tender that he could not lie on his back. Three months after the furuncles had healed, the patient noticed weakness and stiffness in his legs. This progressed slowly and a month later he had to give up work.

The patient was a fairly robust man of middle age. Several scars of old boils were seen over the back; one of these was directly over the spinous process of the seventh thoracic vertebra. Though very spastic he could walk without support with difficulty. Cutaneous sensibility was partially lost below a well defined level crossing just above the umbilicus. Sense of position and vibratory sense were greatly diminished. Bladder control was beginning to be affected. All the tendon reflexes were increased in the legs; there was a bilateral positive Babinski reflex; no abdominal reflexes were obtainable. The spinal fluid was clear and colorless, and there were nine cells per cubic millimeter, all lymphocytes.

At operation a firm fibrous mass was removed from the posterior surface of the dura beneath the laminae of the fifth, sixth, seventh and eighth thoracic vertebrae. The mass was about 1 cm. thick and about 6 cm. long. It did not extend under the anterior surface of the dura. The tumor was recognized to be of inflammatory origin. Cultures were taken and *Staphylococcus aureus* grew therefrom. The wound broke down and healed by granulation. A year later the patient walked almost normally. This case is practically a twin to case 1.

SUMMARY AND CONCLUSIONS

1. In three cases of extradural inflammatory tumors, around which a group of acute and chronic cases have been assembled from the literature, the infections arise either from direct extension of contiguous infections of the soft parts or from hematogenous metastasis of an infection in remote parts of the body.

2. We believe the symptoms of these infections to be sufficiently characteristic to represent a clinical syndrome.

3. The spinal epidural space with its content of fat and areolar tissue determines the presence and location of these infections. This space has no prototype in the cranial chamber; it is situated almost entirely on the dorsal half of the spinal dura; its size varies inversely with that of the spinal cord and cauda equina.

4. Although all the acute infections have run a fulminating and fatal course, except two that were drained, it is hoped that with an early and accurate diagnosis, operative treatment (drainage) may be effectual in saving both life and function.

5. The chronic inflammatory tumors of the epidural space are perhaps more difficult of differential diagnosis than ordinary tumors. It should, however, usually be possible. Their treatment is surgical removal as with any other tumor. The dura should not be opened because of the danger of a renewed infection.

INTUSSUSCEPTION OF THE CECUM COLI

CLINICAL AND PATHOLOGIC REPORT OF A CASE *

KARL H. MARTZLOFF, M.D.

PORTLAND, ORE.

Intestinal intussusception, by no means a common condition in the experience of any one surgeon, has nevertheless received so much attention in all its forms in the literature that an individual case report or a series of case reports is hardly relevant unless an observation is made that may serve to throw some light on the physiology of this process as it occurs in man.

The case reported is unusual in several respects, the most important of which are the apparent incipiency of the process, the pathologic conditions observed and, finally, the possible significance of these in explaining the formation of some forms of pathologic intestinal invaginations.

REPORT OF CASE

History.—D. Y., a white girl, aged 4 years and 4 months, who had been born in Shantung, China, was admitted to the gynecologic service of the Johns Hopkins Hospital, March 29, 1922, under the care of Dr. Thomas Cullen.

The family history was altogether irrelevant. The past history was entirely negative except for the presence of a small umbilical hernia which was noticed, following cord healing, when the patient as an infant strained or cried. This hernia had always reduced spontaneously and had gradually become smaller.

The present illness began eleven days before admission at which time the patient had an upper respiratory tract infection "croup" for which a teaspoonful of "syrup of ipecac" was administered at 10 p. m. with resultant rather severe, but not prolonged "retching." The following morning the child awoke with cramplike pains about the umbilicus, the pains lasting from one to two minutes, followed by an interval of relief lasting from five to fifteen minutes. This condition persisted up to the time of admission, there being an occasional period of emesis which, however, had not been severe. Six days prior to admission some santonin and calomel were given for a possible roundworm infection without producing any change in the symptoms. The father, a physician, states that there had never been any fever, and at no time had there been abdominal tenderness.

Physical Examination.—The temperature was 98.6; pulse, 110; respirations, 24. The white blood cells totaled 13,080. The entire physical examination, including the stool examination, was irrelevant except for the abdominal findings. There was a definite umbilical defect which admitted the tip of the small finger. When the patient coughed a definite tumefaction was seen and a well marked cough impulse was felt. Nothing to suggest incarceration or

---

* From the department of gynecology of the Johns Hopkins Hospital and University.

strangulation of the abdominal contents was noted. The abdominal respiratory movements were normal and there was no tenderness, rigidity or muscle spasm.

The preoperative impression was that the patient had an umbilical hernia which would be reducible, possibly a Meckel's diverticulum with partial intestinal obstruction.

Operation.—Dr. Cullen operated, March 30. Abdominal exploration was easily performed, no abnormalities being noted except for the cecum. Here on its antero-lateral aspect, including the lateral half of the anterior taenia coli, was seen a round defect sufficiently large to admit the tip of the index finger for about 2 cm. On palpation a small mass could be felt through the wall of the cecum

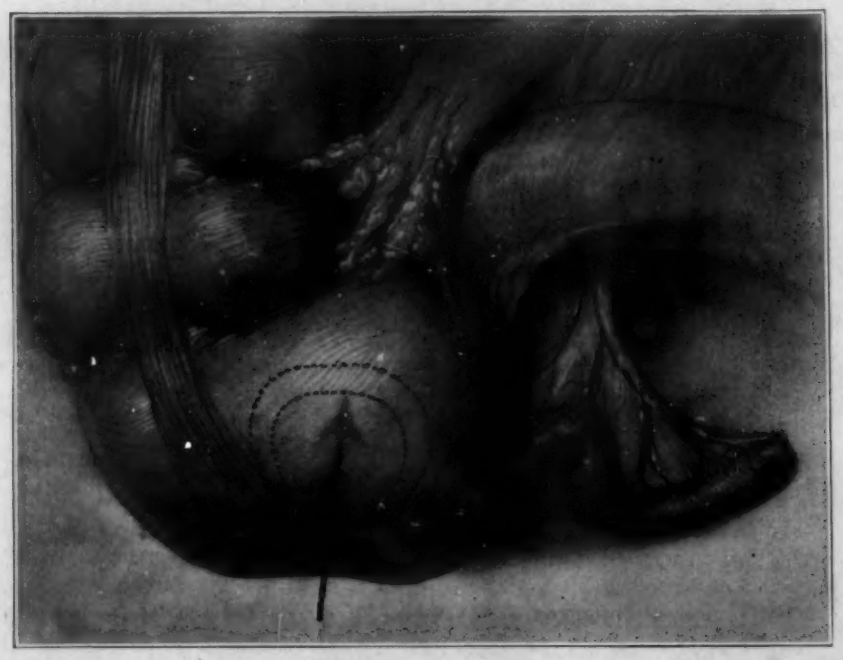


Fig. 1.—Situation of cecal invagination in relation to appendix and anterior taenia coli.

apparently attached to the intestinal wall at the point where the defect, just mentioned, existed.

Figures 1 and 2 represent in a semidiagrammatic manner the condition found at operation. Pressing on the anterior and medial aspect of the cecum caused the mass to vanish, and simultaneously an invagination to unfold, bringing to view the serous aspect of the invaginated portion which appeared hyperemic, somewhat roughened, and possibly slightly puckered. On palpation this area felt of cartilaginous consistency. One lymph gland at the anterior-superior aspect of the ileocecal junction was definitely enlarged, elastic and smooth. The neighboring mesenteric glands showed no macroscopic change. The ileum and cecum elsewhere appeared normal while the appendix showed some dilatation of its subserous vessels.

The pathologic area in the cecum was excised, a flexible curved Kocher intestinal forceps being applied so as to prevent the intestinal contents from soiling the operative field. The defect was closed with two rows of No. 2 plain catgut, the appendix was removed and the abdominal wall closed in layers, one small drain of protective material being left in situ and removed after twenty-four hours.

The patient's convalescence was uneventful. She left the hospital on the eighth day following the operation and is now living and well after three years, no recurrence of symptoms having been noted.

Pathologic Examination.—The gross specimen consisted of a small piece of tissue, somewhat irregular in outline, measuring 2.5 by 3 cm. and from 4 to 6 mm. in thickness. On one surface (serosa) the tissue was pale gray, smooth

Fig. 2.—Schematic drawing of cecum in coronal section showing relation of invaginated portion to orifice of vermiform appendix and ileocecal valve.

and glistening. On the other surface (mucosa) there was an elevated central area, about 12 mm. in diameter, which was purplish red, opaque and dull in appearance and on palpation was rather firm in consistency. No exudate was seen. On section the cut surfaces were smooth and dark purple for a depth of from 2 to 3 mm.; beyond this point the tissue in its remaining thickness was pale gray and glistening. The area just described was surrounded by a narrow zone of pale gray, glistening and delicate mucosa, which was about normally movable on its underlying structures.

Microscopic sections were made of tissue fixed in Zenker-formaldehyde solution and stained with hematoxylin and eosin. Sections from the less abnormal areas at the periphery of the specimen showed the large intestine, the epithelium of which appeared essentially normal except for one area where a thin layer

of overlying exudate (just to the left of *X* in figure 3) was seen. Beneath this exudate the superficial mucosa cells showed definite impairment in staining reaction. There was moderate extravasation of red blood cells into the interglandular stroma of the mucosa; some large round wandering cells were present, and here also hyaline thrombi situated in the capillaries were not infrequent. The submucosa showed considerable edema and in its superficial portion a considerable infiltration with polymorphonuclear eosinophils and erythrocytes. The tunica muscularis was quite distinct and apparently unchanged except that it (both circular and longitudinal layers) together with the subserosa showed a characteristic appearance of edema. The serosa was intact.

As one approaches the area beneath *X* in figure 3 one notes a gradual intensification of the process described above. At *X* an abrupt transition occurs marked by hemorrhage in the submucosa and complete obliteration of the architecture of the mucosa, muscularis mucosae and the superficial half of the submucosa, these now being represented by a pink staining, reticular mass. In the most superficial portion of this necrotic process no cellular elements are

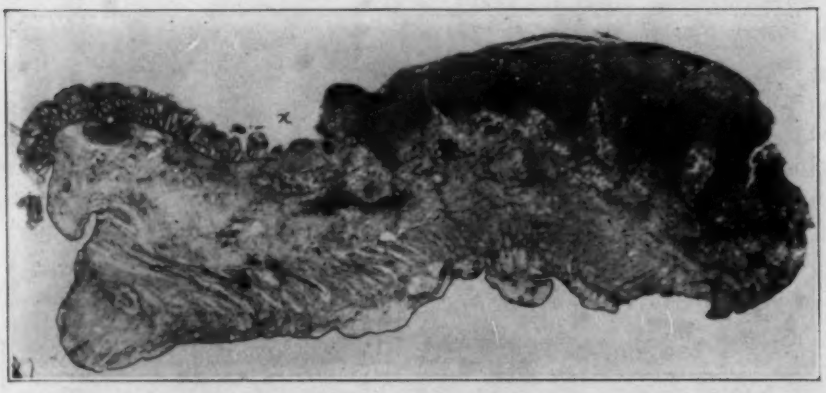


Fig. 3.—Microsection of intestine (×9.6) showing, to left of *X*, some edema and only a moderate degree of cellular infiltration, the latter being limited to the mucosa and submucosa and at *X* an abrupt change, which, at the extreme right of the section, involves the entire thickness of the intestine in a necrotic process; the right margin of this section represents the midportion of the necrotic zone and corresponds to the midpoint of the apex of the invagination in figure 2.

seen. Beneath this acellular zone a zone of dense round cell infiltration occurs, a few polymorphonuclear leukocytes are also present, and an occasional capillary containing a fibrinous thrombus is seen. The fibers of the tunica muscularis, both circular and longitudinal, show marked impairment in staining reaction and indistinctness in outline. There is little if any cellular infiltration here or in the subserosa which, however, shows evidence of marked edema.

Sections stained for connective tissue by both Mallory's and van Gieson's methods showed no increase in fibrous stroma.

Sections stained for bacteria by a combination of Goodpasture's and Weigert's stains as described by MacCallum[1] showed here and there a super-

1. MacCallum, W. G.: A Stain for Influenza Bacilli in Tissues, J. A. M. A. **72**:193 (Jan. 18) 1919.

ficial area in the necrotic tissue in which some gram-positive cocci and large, broad bacilli and many small gram-negative bacilli were seen. The deeper portions of the necrotic zone and the remaining thickness of the intestinal wall contained no demonstrable bacteria and no protozoa were seen.

The groups of ganglion cells lying between the layers of the tunica muscularis and those occurring in the submucosa, in the less abnormal portions of the intestinal wall, possessed normally staining elements. Their nuclei contained the usual well defined and markedly chromophilic nucleoli and there was a well defined nuclear membrane surrounded by an ill defined cytoplasm which took a faint eosin stain. As one approached the more pathologic portion of the intestine one was impressed by the ability of these neurologic elements to retain their morphology, though their staining properties were somewhat impaired, while the surrounding muscle fibers showed distinct loss of outline and lessened staining reaction. In those portions of the sections showing the most advanced pathologic change neurologic elements could no longer be identified.

The pathologic lesion described in the foregoing is explainable, we believe, leaving out of consideration for the present the mechanism of the invagination, as the result primarily of a purely mechanical process, namely, the interference with the circulation to the invaginated portion of the cecum, with its consequent series of tissue changes resulting successively in edema, necrosis and thrombus formation, peripheral cellular infiltration and extravasation and, finally, in *superficial* invasion of the necrotic mucosa by bacteria of the intestine. In short, the process partakes of the nature of an infarction.

Particular attention is invited to the fact that the most advanced pathologic changes are present at the apex of the invagination and that the central portion of the apex shows the most extensive change of all in that the entire thickness of the intestine shows evidence of degeneration, lessening in degree, however, from within outward. The remainder of the invaginated intestine, from the apex peripherally, shows a corresponding decrease in edema and cellular infiltration.

The frequency of occurrence of a pure cecal type of intussusception is difficult to estimate from a most extensive review of the literature owing to the fact that by far the greater number of reports represent pure clinical observations, in which histologic examinations form the exception rather than the rule and accurate detailed descriptions of the operative findings are not recorded. For example, Rushmore,[2] in a review of 237 cases, reports only two instances of a cecal type of intussusception. On the other hand, Hipsley,[3] in a study of forty cases in which the origin of the intussusception was noted, reports nineteen in which the process began at the tip of the cecum "just above the junc-

2. Rushmore, J. D.: Intussusception, Ann. Surg. **46**:210-223, 1907.

3. Hipsley, P. L.: A Résumé of Fifty-One Cases of Intussusception, M. J. Australia **2**:383-386 (Nov. 9) 1918.

tion of the anterior and lateral taenia coli." Likewise Clubbe,[4] referring to the place of origin of invaginations, in a most careful study of his findings in 100 consecutive operations for intussusception in children, notes that in the ileocecal variety of intussusception the starting point is in the caput caeci and not at the valve, as is generally assumed to be the case. This free end of the cecum is often a little difficult to unfold, after the reduction of the main part of the intussusception, remaining as a "small cup-shaped depression with hard walls." Clubbe in his remarks on intussusceptions beginning in the ileum notes also that the first infolding seems to start at the side of the bowel and always opposite the mesenteric attachment.

Joyce [5] reports in detail a case of advanced intussusception which on reduction showed "the end of the cecum inverted, thick and hard," forming on palpation a "button-like structure," it being necessary to "knead" the cecum to restore it to its proper shape. Thomas [6] reports a case probably less advanced than any of those preceding. This occurred in a boy of 13; the end of the cecum was invaginated, having carried in with it that portion to which the appendix was attached. The walls of the cecum were much thickened owing to edema, but the ileocecal valve was not involved. Possibly the earliest instance encountered is one reported by Shacklock.[7] From his description it probably resembles more closely than any of the others the case that forms the motif for this paper. Shacklock's patient was a boy, aged 7 years, in whom the cecum just lateral to the vermiform appendix had invaginated the remainder of the cecum in an upward direction for about 1 inch (2.5 cm.). In the foregoing reports, unfortunately, no pathologic descriptions are given other than those observed at operation.

Shacklock's case is the only one encountered in the literature which in its apparent incipiency resembles closely the case reported in this article, and it is particularly regrettable that no histologic study was available; however, manipulation was sufficient in this case to reduce the invagination, appendectomy was performed and the patient made an uneventful recovery.

A case reported by Cole [8] is given here in considerable detail, because the tumor that he describes as accompanying the intussusception most closely resembles the microscopic appearance of the diseased section

---

4. Clubbe, C. P. B.: One Hundred Consecutive Laparotomies for Intussusception in Children, Brit. M. J. **1**:1327, 1905.

5. Joyce, C.: An Unusual Form of Intussusception, M. J. Australia **2**:540, 1914.

6. Thomas, T. T.: Intussusception of Head of Cecum Without Involvement of Ileocecal Valve, Tr. Philadelphia Acad. Surg., 1918-1919, **21**:110, 1920.

7. Shacklock, G. A. S.: Three Cases of Intussusception, Guy's Hosp. Gaz. **31**:36, 1917.

8. Cole, A. F.: A Case of Intussusception (Cecocolic) and Remarks on the Pathology of the Accompanying Tumor, China M. J. **22**:13-16, 1908.

found in our case, though the intussusception was well advanced in Cole's case and could, therefore, hardly be considered incipient.

Cole's case is one of cecal intussusception, about 8 inches (20.3 cm.) of the cecum and ascending colon being found within the more distally situated ascending colon. Reduction was easily performed, the cecum and appendix coming into view when reduction had been completed. Near the base of the appendix the walls of the cecum were puckered, hard and thick. This area, with the appendix, was excised and a tumor mass presented, projecting about one-half inch (1.27 cm.) into the intestine. The mass was greenish black in appearance, smooth and about seven-eighths inches (2.1 cm.) in diameter. Microscopically, "it was seen to consist in the main of widely dilated spaces filled with leukocytes, red cells, and in places with a colloid material perhaps of lymphatic origin. There is marked round celled inflammatory infiltration at the margin of the growth." . . . "The surface of the tumor is smooth and the ordinary glandular nature of the cecal mucosa is replaced by a homogeneous mass of disintegrating cells with different staining properties from the deeper portion. Here and there a suggestion of the original tubular nature can be seen. . . . The muscularis mucosae is somewhat atrophic but there is no evidence of malignant invasion."

Cole considers the inflammatory process in his case as primarily mechanical in etiology due to some constricting process, and ventures the suggestion of a reverse peristalsis causing this portion of the cecum to become engaged in the orifice of the ileocecal valve.

It would appear that Cole's case is altogether similar to the one reported in this article and that the inflammatory tumor he describes probably had its origin in an identical manner.

Cases described as invagination of the cecum due to inflammation at the base of the appendix such as reported by Rogers,[9] Wright and Knowles,[10] together with another group of cases described by Struthers,[11] Brown,[12] Connor,[13] Monsorrat,[14] Rolleston,[15] Waterhouse[16] and others

9. Rogers, J. T.: Invagination of the Bowel Due to Inflammation at the Base of the Appendix, St. Paul M. J. **11**:458-463, 1909.

10. Wright, G. A., and Knowles, R.: Chronic Intussusception of the Appendix into the Cecum: Operation; Recovery, Brit. M. J. **1**:1470, 1897.

11. Struthers, J. W.: A Case of Chronic Intussusception with Complete Inversion of the Vermiform Appendix, Lancet **2**:1345, 1906.

12. Brown, W.: A Case of Intussusception of the Vermiform Appendix, Scot. M. & S. J. **12**:333-335, 1903.

13. Connor, F. P.: Intussusception of the Vermiform Appendix, Lancet **2**:600, 1903.

14. Monsorrat, Keith: Intussusception of the Vermiform Appendix, Liverpool M.-Chir. J. **21**:68-78, 1901.

15. Rolleston, H. D.: Prolapse of the Mucous Membrane of the Appendix into the Cecum, Edinburgh M. J. **4**:21-26, 1898.

16. Waterhouse, H. F.: Intussusception of the Vermiform Appendix, Brit. M. J. **2**:1505, 1897.

as intussusceptions of the vermiform appendix, are interesting and may properly be mentioned here, for they are mere variations in situation and extent of the same process and our case is probably illustrative of them all as they appeared in their incipiency.

Masson and Leriche [17] report an interesting case of a chronic "ileo-caecocolique invagination." It is mentioned here because of the careful histologic study made and on account of their interpretation of the pathologic findings. The specimen described was removed from a young Arab at operation and consisted of the cecum, a portion of the ileum, and a portion of the ascending colon. Three areas of ulceration were noted in the cecum and are described as resembling dysenteric (dysentériformes) ulcers, though none of the specific pathogens that produce the more frequent forms of infectious ulcerative intestinal lesions are demonstrated. The ulcers present nothing unusual, there being a central loss of substance with a surrounding subacute inflammatory reaction, and they are sufficiently deep to involve the muscularis. The intestinal wall intervening between those three discrete areas of ulceration is not noteworthy except for some edema. The authors draw particular attention to the plexuses of Auerbach and Meissner, showing that except where directly involved in the ulcerations or their dense surrounding inflammatory reaction, the plexuses are histologically normal. Sections of the ileum and ascending colon are not noteworthy, except for some edema and hyaline change in the ileum. This case of Masson and Leriche is lengthily recited because the authors consider the cecal ulcerations as the primary factors in the chronology of events: to quote "Que les ulcerations dysentériformes doivent etre considérées comme primitives." The histopathology of the lesions they described differs from our case and that of Cole's in that their lesions have been of longer duration, with ulceration and evidence of beginning organization in the surrounding inflammatory zones, as indicated by the formation of new capillaries, etc. We feel that the lesion described by us, if encountered at a later date, would also have shown a loss of substance in the zone occupied by the necrotic material and that evidence of tissue repair would undoubtedly have been demonstrable at a later stage. In brief, the difference appears to be one of degree and not of quality.

In a brief consideration of the theories regarding the physiologic pathology of intestinal intussusception in the absence of tumors, diverticula, etc., two often quoted opposing schools may be regarded: one attributing the beginning of an intussusception to a primary localized area of intestinal spasm, the other to a primary area of intestinal paraly-

17. Masson, P., and Leriche, R.: Recherches sur la physiologie pathologique de l'invagination intestinale chronique, Lyon chir. **16**:325-343 (May-June) 1920.

sis. Nothnagel [18] is probably the most vigorous proponent of the former theory while Peyer (quoted by Kasemeyer [19] and Leubuscher [20]) and Leichtenstern [21] espouse the latter hypothesis, which is the older. Both Nothnagel and Leubuscher have been unable to demonstrate experimentally the paralytic mechanism of intestinal invagination. On the other hand, Nothnagel by the use of the faradic current on the rabbit intestine has produced a tetanic contraction of a circumscribed portion of intestine. At the point where the contracted intestine and the caudad normal portion join, Nothnagel noted a small invagination formed by the normal distal segment of the intestine drawing itself up over the distal portion of the contracted portion in an umbrella-like manner. The further formation of the invagination occurred at the expense of the distal segment of intestine. Nothnagel feels that after the invagination is well developed the tip of the intussusception, which is then well in confines of the distal intestinal segment, acts as any other intestinal content, exciting peristalsis and causing propulsion of the intussusceptum analward. In this regard it may be mentioned that Treves (quoted by Nothnagel) accepts Nothnagel's view and a case reported by Rushmore [2] in a child of 9 also confirms in part this explanation. Operation on Rushmore's patient disclosed a well developed intestinal intussusception. After partial reduction had been effected manual traction was interrupted for a moment. In this interval Rushmore noticed that the intussusception began to reform by the intussuscipiens sliding up over the intussusceptum instead of the intussusceptum gliding down into the intussuscipiens as is usually regarded as the mechanism.

A case reported by Veau [22] would also seem to bear out in part Nothnagel's theory clinically. Veau's case occurred in a male infant of 5 months on whom he had operated for an intussusception by resecting the cecum. Thirty-six hours after operation the patient again began to develop symptoms of intestinal obstruction. At the second operation Veau found about 50 cm. of the small intestine tightly contracted and firm. During this observation the author saw two invaginations of about 1 cm. occur at either end of the constricted intestine, but he does not describe their mechanism. He concludes, however, that spastic contraction is essential before intussusception can occur.

---

18. Nothnagel, H.: Specielle Pathologie und Therapie, Vienna, A. Holder, 1903, **17**:385-417.

19. Kasemeyer, E.: Tumorinvagination des darms, Deutsche Ztschr. f. Chir. **118**:205-264, 1912.

20. Leubuscher, G.: Experimentelle beiträge zur aetiologie der darminvagination, Virchows Arch. f. path. Anat. **85**:83-94, 1881.

21. Leichtenstern, O.: Ueber darm-invagination, Prager Vierteljahrschr. f. prakt. Heilk. **2**:189-221; **4**:58, 1873.

22. Veau, V.: Le spasme intestinal comme cause d'invagination, Bull. Soc. de pédiat. de Paris **8**:424-428, 1906.

The production of reversed intestinal peristalsis by the use of sodium carbonate [23] is also confirmatory of Nothnagel's observation. The application of sodium carbonate to the serous aspect of the intestine produces, according to Morris, a pronounced tonic spasm followed by intussusception of the contracted portion by reverse peristalsis of the caudad lying intestine.

A suggestive experimental observation has recently been made by Alvarez [24] in the small intestine of the cat showing how antiperistalsis may occur without explainable cause. The observance of antiperistalsis with obstruction is, of course, not uncommon, while in the large intestine its occurrence without obstruction is physiologic.

There are, of course, other subscribers to the spasmodic theory, principally Brinton and Rafinesque (quoted by Nothnagel), who explain the further development of the intussusception in a somewhat different manner.

Peyer and Leichtenstern, while both embracing the hypothesis that a primary zone of intestinal paralysis is the preliminary requirement before intussusception can occur, nevertheless differ as to the process whereby the intussusceptum and intussuscipiens form. The details of this are probably irrelevant to this discussion. A recent clinical instance that is construed as supporting the paralytic theory of intussusception formation is reported by Syring.[25] This author reports a case of intussusception observed during the recent World War in a soldier with a gunshot wound of the abdomen. Operation revealed, in addition to several intestinal perforations, an injury to the mesentery of the jejunum. At the exact level of the mesenteric injury the operator noted a complete intussusception, 8 cm. long, easily reduced and covered with a layer of fibrin. Syring feels that the mesenteric injury severed a branch of the superior mesenteric artery and an accompanying nerve, a branch of the superior mesenteric plexus, in this way depriving this segment of intestine of its vagus innervation and possibly also of its splanchnic nerve supply. This series of events the author feels caused a localized area of intestinal paralysis, thereby fulfilling the primary requirement for the formation of the intussusception which he discovered at operation.

We feel that the case reported in this article is an instance of partial cecal intussusception occurring in a portion of the cecum where, if one

---

23. Morris, R. T.: The Production of Ileal Intussusception with Carbonate of Sodium, M. Rec. **45**:389, 1894.

24. Alvarez, W. C., and Mahoney, L. J.: Peristaltic Rush in the Rabbit, Am. J. Physiol. **69**:211-225 (July) 1924.

25. Syring: Ein beitrag zur nervenpathologie des darmes und zur pathogenese der intussuszeption, Beitr. z. klin. Chir. **114**:131-137, 1918.

may judge from the literature, cecal intussusceptions are prone to originate.

The formation of the invagination in this particular instance, we assume, is best explained by the occurrence of abnormal intestinal excitation following the ingestion of some ipecac, which in turn caused severe and ineffectual attempts to vomit. As part of the intestinal reaction an area in the cecum underwent abnormally prolonged contraction so that when relaxation did occur a portion of the contracted intestine had undergone a localized edema, due to some degree of circulatory stasis. In this way an invagination persisted and its spontaneous reduction was no longer possible. After this primary invagination and edema, the invaginated portion acted much as a foreign body; it excited intestinal peristalsis with consequent traction on the invaginated area which resulted in further circulatory embarrassment, finally producing at the apex of the invaginated portion an area showing the varying degrees of damage that may follow a prolonged ischemia. This is well brought out in part of figure 3 where the mucosa, muscularis mucosae and the superficial portion of the submucosa form a structureless necrotic area. Peripheral to this, in addition to the inflammatory reaction one sees the remaining submucosa very edematous and both layers of the tunica muscularis show definite degeneration, as evidenced by loss of cell outline and the impaired staining reaction of their component muscle fibers as previously described. The whole picture in fact is similar to some of the pathologic appearances first described by D'Arcy Power [26] in his article on the minute anatomy of intussusception.

The normal appearance of the ileum and all other portions of the large intestine rather speak against their participation in this process. To fulfil Leichtenstern's hypothesis one should have sufficient intestine proximal to the invaginated area, which would represent the segment of paralyzed intestine, to propel the latter into the caudad intestinal segment.

Obviously the cecum without the ileum could not afford this propelling force, owing to the situation of the invagination. There is no evidence that the ileum supplied this want for there is nothing to indicate an ileocecal invagination, which would have been necessary to allow the remaining proximal portion of the cecum to participate.

Reverting to Nothnagel's explanation of intussusception in the absence of tumors and diverticula, we feel that in our case his first postulate has probably been fulfilled; namely, an area of intestinal spasm has most likely occurred. Whether the caudad segment of large intestine drew itself up over this area of constriction one cannot say.

---

26. Power, D'Arcy: Some Points in the Minute Anatomy of Intussusception, J. Path. & Bact., June, 1897.

It does not, however, seem probable that a portion of the circumference of the intestine would undergo antiperistalsis in such a manner as to provide an invagination such as this, for intestinal movement is usually circumferential even when antiperistaltic. However, at operation nothing could be noted that might suggest a participation of the neighboring large intestine in an intussusception. Indeed, the remainder of the circumference of the cecum at the level of the invagination appeared normal. We therefore feel that we are in the presence of an incomplete and probably incipient form of cecal invagination which represents one of the early stages of more advanced forms of cecal intussusception reported in the literature as arising in this particular situation; that is, near the point of convergence of the anterior and lateral taeniae coli. From pathologic evidence at hand we believe that an unusual contraction of the wall of the cecum in this particular segment provided the beginning for a series of events resulting in the invagination described. Furthermore, it seems reasonable to assume that this may have occurred without participation of the distal lying segment of the intestine as postulated by Nothnagel, or by a mechanism such as that described by Leichtenstern.

One naturally wonders whether processes such as that observed in this case, possibly not even so far advanced, are not of more frequent occurrence than is generally supposed. In fact, it is possible that such conditions unless carefully searched for may be overlooked at operation, the condition correcting itself through manipulation and the subsequent freedom from symptoms attributed to the removal of a macroscopically "suspicious looking" but a histologically normal appendix.

TORSION OF THE GREAT OMENTUM PRODUCING SYMPTOMS SIMULATING ACUTE APPENDICITIS *

J. WILLIAM HINTON, M.D.

Associate in Surgery at New York Post-Graduate Medical School and Hospital; Adjunct Assistant Visiting Surgeon, Bellevue Hospital

NEW YORK

This subject has recently been reviewed by Mullen,[1] but the case reported here presents findings that are not in accord with most of the previously reported cases. Reidel,[2] quoted by Fuller,[3] says, "Given an instance in which the normal omentum is free from pathology of whatever kind, torsion or rotation would probably never occur." Mullen classifies torsion of the omentum into three kinds.

1. Torsion in cases in which the omentum has in its distal end a mass that is free or has become free through twisting. Luckett[4] says, "Nearly every case of reported torsion of the omentum was associated with some form of inflammation, either within or without the abdomen, as in a hernia." Mullen thinks hernias play an important rôle in the causation of omental torsion, as is evident from the large percentage of reported cases in which there has been an associated hernia. It is usually the right inguinal variety which has been of long standing and is usually reducible. He quotes Vignard and Girandeau[5] as having reported twenty cases of torsion, in which inguinal hernia was present in nineteen. It may be due to the constant entrance and exit of the omentum into the hernial sac, with irritation and thickening of the lower end.

2. Torsion in cases in which the distal end of the omentum is adherent in the hernial sac or about an inflammatory area. In this type of torsion, the tip of the omentum being adherent in the pelvis because of an inflammatory process, such as a suppurating tube, acute appendicitis or hernial sac, the organ becomes a sort of sling and rotates as one may twist a handkerchief by grasping it at opposite corners and twirling.

---

* From the surgical service of Dr. Charles Gordon Heyd at New York Post-Graduate Medical School and Hospital.

1. Mullen, T. F.: Torsion of the Great Omentum, Surg. Gynec. Obst. **40**: 635 (May) 1925.

2. Reidel: München. med. Wchnscshr. **41**, 1905.

3. Fuller, W.: Intra-Abdominal Rotation of the Great Omentum Unaccompanied with Hernia, Surg. Gynec. Obst. **7**:231-243, 1908.

4. Luckett, W. H.: Torsion of the Greater or Gastrocolic Omentum, J. A. M. A. **54**:1364 (April 23) 1910.

5. Vignard, E., and Girandeau: Torsion intra-abdominal du grand epiploon, Arch. prov. de Chir. **12**:206-230, 1903.

3. Cases in which apparently free omentum twists without being the site of a mass or being adherent in the pelvis. Payr [6] says that this variety presumably is due to the fact that the veins are larger and more tortuous than the arteries and that when the veins are compressed by a kink of some kind they become turgid and full of blood; the arteries form a tense cord about which the omentum turns and once started to twist

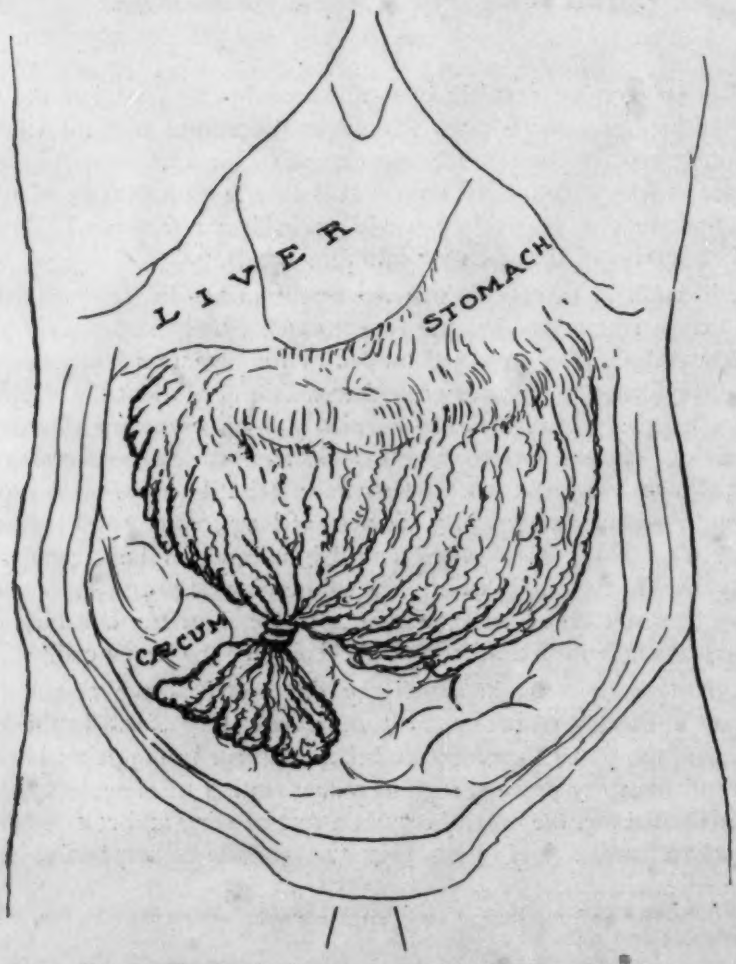


Fig. 1.—Torsion in the omentum (diagrammatic sketch).

continues with resulting obstruction to the circulation and subsequent gangrene. The following case belongs to group 3 as no etiologic factor was found to explain the torsion. There was no evidence of hernia or pelvic infection, and the appendix showed no macroscopic evidence of

6. Payr: Arch. f. klin. Chir. **67,** 1902.

disease. The patient had a chronic cholecystitis and cholelithiasis but there were no adhesions or bands in the upper part of the abdomen. Figure 1 is a diagrammatic sketch of the torsion in the omentum. Figure 2 shows three complete twists in the omentum.

REPORT OF CASE

A woman, aged 28, had had pains in the abdomen for eighteen hours. She had had no serious illnesses or surgical operations; two children, aged 6 and 4

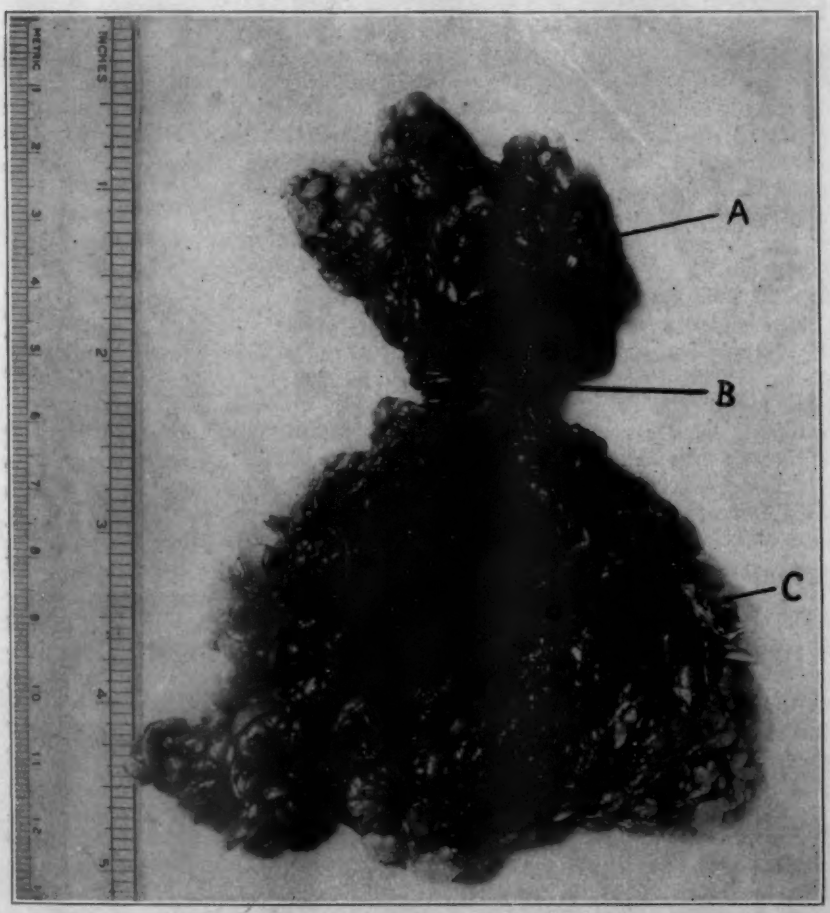


Fig. 2.—*A*, normal omentum; *B*, three twists in omentum; *C*, gangrenous omentum.

years, were alive and well. She had no puerperal infection. She had been bothered with indigestion and vague pains in the upper part of the abdomen after eating for several years. This pain was different from the one she was complaining of at the present time. She attributed it to an affected gallbladder and gallstones, as her husband had the same symptoms, for which he had an operation.

Her menstrual periods were regular and came every twenty-eight days. The last period had been two weeks before admission.

The patient stated that eighteen hours before admission she was seized with pains in the region of the umbilicus and that after a few hours she vomited. The pain later became localized to the right lower quadrant. It was severe enough to keep her awake most of the night. A doctor was called eight hours after the onset of the pain and diagnosed her condition as acute appendicitis. An operation was advised. The patient was out of town and refused as she preferred to return home. The pain continued but chiefly in the right lower quadrant, at which place she complained of considerable tenderness.

Physical examination showed a woman confined to bed apparently suffering from acute pain in the abdomen. The temperature was 99, the pulse 80. The throat was negative for tonsillitis or pharyngitis. The chest was normal. On abdominal examination there was no tenderness over the left or the right upper quadrant. There was a marked tenderness over the right lower quadrant at McBurney's point and a slight rigidity in this region. The tenderness seemed out of proportion to the pain of which she complained. There was no costovertebral tenderness on either side. Vaginal examination showed the fornices normal. No masses were felt. The uterus was normal.

Urinalysis was negative. The leukocyte count was 17,000; polymorphonuclear neutrophils, 74 per cent; small lymphocytes, 19 per cent; large lympocytes, 5 per cent, and transitionals, 2 per cent.

The preoperative diagnosis was acute appendicitis.

The abdomen was opened through a right rectus incision, under ether anesthesia. When the peritoneum was opened, the hand was inserted to the right lower quadrant and a mass containing gangrenous omentum was encountered and delivered. This was not inspected carefully but was wrapped in abdominal pads. The cecum was then delivered and the appendix showed no evidence of acute infection. An appendectomy was performed, the stump of the appendix being carbolized and inverted. The upper part of the abdomen was palpated and the gallbladder was found to contain one large stone. The omentum was then inspected and it was found to have the lower portion twisted on itself three times. No masses were felt in the omentum. The mass of gangrenous omentum was then excised, about 1 inch (2.5 cm.) of healthy omentum above the twist being removed. The incision was enlarged upward and the gallbladder was found to contain one large stone, with no evidence of acute infection. A cholecystectomy was performed. The common duct was negative for calculi. A rubber tissue drain was inserted to the space in front of the right kidney, known as Morrison's space, and the abdomen was closed in layers.

The pathologic report stated that the gross specimen measured 110 by 90 mm. It was twisted in the middle. The lower part was hemorrhagic. Microscopic examination of the sections showed fat tissue that was hemorrhagic. The blood vessels were engorged and partly thrombosed, with slight infiltration of the fat tissue by polymorphonuclear leukocytes.

The patient made an uneventful recovery and was discharged from the hospital on the twelfth day.

125 East Seventy-Second Street.

THE VALVES OF HEISTER*

STANLEY H. MENTZER, M.D.

Fellow in Surgery, the Mayo Foundation

ROCHESTER, MINN.

In 1732 Laurentius Heister [1] first described the valvular arrangement of the mucous membrane of the cystic duct that bears his name. He attributed to these leaflets projecting into the cystic duct a functional rôle of the gallbladder, namely, the storage of bile. Recent studies are at variance with this hypothesis; for this reason I undertook an anatomic and experimental study of the problem in 1923.

The mucous folds in the cystic duct apparently reach their highest development in man. They are present in the dog, rabbit and a few other animals, but are less developed and fewer in number. A study of the comparative anatomy, therefore, suggests the very minor part played by these leaflets in the functional activity of the gallbladder. Indeed, in many species there are no leaflets and this must be considered in attempts to ascribe a functional rôle to the valves. Certainly their absence lessens the significance of any functional activity that might be credited to them in man. It does not seem likely that the valves of Heister are vestigial in man, for if they were the leaflets presumably would be better developed in the lower animal forms.

ANATOMY

The cystic duct in man is not of constant shape or size. It has been variously described as "kinked," "bassinet-shaped," "sharply flexed on itself," "S-shaped" and "double mesial curved" (figs. 1 and 2). In a series of 612 cystic ducts examined at necropsy, only nineteen were true S-shape; forty-one were single curves sharply flexed on themselves. In five instances, however, the duct was devoid of curves or flexions and appeared as a straight duct in gallbladder specimens free from gross pathologic changes (figs. 3 and 4).

Schmieden [2] has pointed out that in most cases the cystic duct leaves the gallbladder at the side and not at the most proximal portion of the

---

* Work done in the Section on Pathologic Anatomy, Mayo Clinic.

1. Heister, L., quoted by Schmieden, V.: Ueber die "Stauungsgallenblase," Zentralbl. f. Chir. **47**:1257-1261, 1920.

2. Schmieden (footnote 1). Schmieden, F., and Rohde, Carl: Die Stauungsgallenblase mit besonderer Berücksichtigung der Ätiologie der Gallenstauungen, Arch. f. klin. Chir. **118**:14-53, 1921.

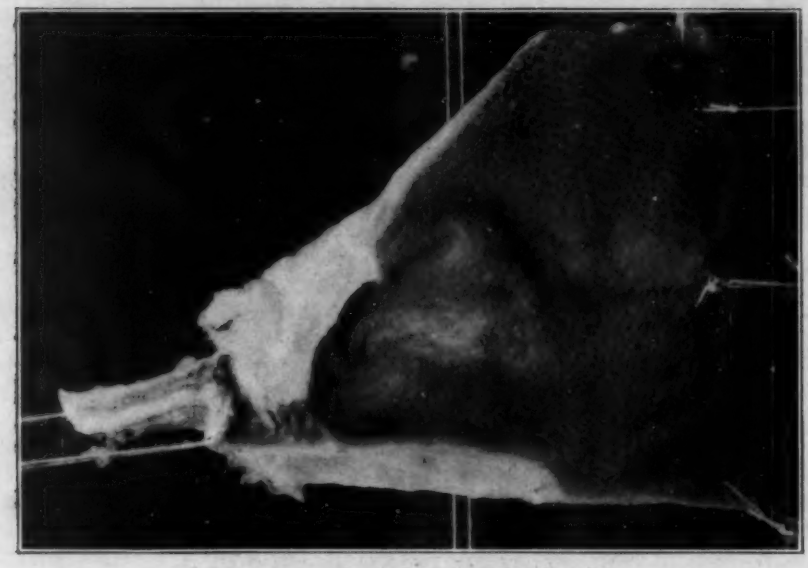


Fig. 1.—S-shaped cystic duct.

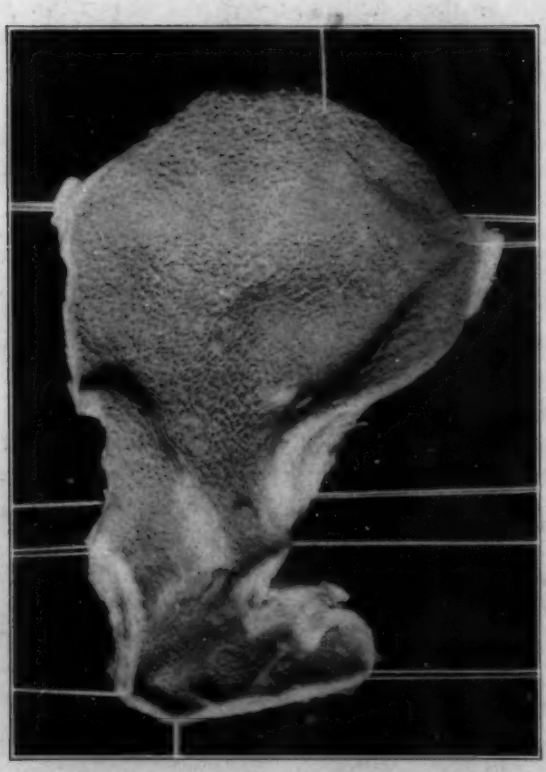


Fig. 2.—Bassinet-shaped cystic duct, two leaflets only constituting valves of Heister.

organ. I also observed this. Jacobson and Gydeson [3] believe that the cystic kink, which is frequently present close to the emergence of the cystic duct from the gallbladder, is concerned in the emptying of the organ. They assert that the gallbladder can be distended almost to the

Fig. 3.—Straight cystic duct.

Fig. 4.—Straight cystic duct.

bursting point without forcing bile out of the cystic duct, whereas it can be easily emptied by slight longitudinal traction on the duct. They believe that the valvular action of the cystic kink is thereby lessened.

3. Jacobson, Conrad; and Gydeson, Carl: Function of the Gallbladder in Biliary Flow, Arch. Surg. **5**:374-394 (Sept.) 1922.

German pathologists lay much emphasis on the stagnation of bile produced by this angulation of the cystic duct as an etiologic factor in the formation of gallstones. From my study I was led to believe that such mechanical causes of obstruction to the flow of bile must be relatively rare.

Fig. 5.—Valvular arrangement in cystic duct.

Fig. 6.—Cholesterosis of gallbladder, with no leaflets in lower two-thirds of cystic duct.

The valves of Heister are projections of mucous membrane into the lumen of the cystic duct. They line the course of the duct more or less completely, being larger and less numerous at the distal end and

smaller and more abundant at the common duct terminus of the cystic duct (fig. 5). There are, however, many variations in this distribution. In three of our series of 612 cases there were no leaflets in the lower third of the cystic duct (fig. 6). In one case the first leaflet began almost a fourth of the way up the gallbladder from the cystic duct.

The leaflets are arranged more or less spirally, running in a clockwise direction down the cystic duct from its origin at the gallbladder. The majority of the leaflets extend from one-half to three-quarters of the way around the duct. The leaflet above and below overlaps the intermediate valve to a greater or less extent. In many instances the leaflets make a complete circuit of the duct, and in several of the cases

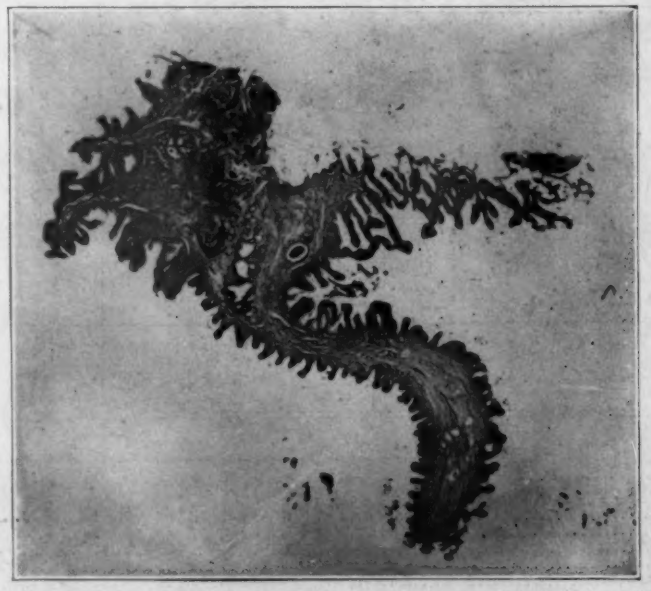


Fig. 7.—Section of leaflet of valves of Heister (×15).

in this study a single leaflet made two complete turns around the duct. Hartmann [4] and Faure,[5] in their early descriptions, pointed out that the duct is not a spiral canal, but that it is a duct interrupted by incomplete spiral leaflets in its course. They pointed out that the upper leaflets sometimes extend three-quarters of the way around the duct, and for this reason the duct is impassable to a probe or other solid object. Terrier and Dalley [6] agreed with these contentions and made copper

4. Hartmann, quoted by Jacobson and Gydeson (footnote 3).

5. Faure, J. L., quoted by Jacobson and Gydeson (footnote 3).

6. Terrier, F., and Dally: Du cathétérisme des voies biliaires, Rev. de chir. **12**:136-168, 1892.

models of the leaflets. Brewer [7] likewise found the cystic duct impassable to a probe in all but ten of ninety-seven cases; I succeeded in passing a probe in only sixteen of 198 normal gallbladders. Of this number eight possessed no leaflets nor other suggestion of valves of Heister.

The number of leaflets comprising the valves varies greatly (table 1). In a series of 338 essentially normal gallbladders, in which there were no gross evidences of inflammatory changes and no gallstones or evi-

TABLE 1.—*Leaflets Comprising the Valves of Heister*

Normal Gallbladders		Essentially Normal Gallbladders (Cholesterosis)		
Leaflets	Cases	Leaflets	Cases	Total
..	8	..	..	8
1	5	1	.	5
2	13	2	4	17
3	29	3	10	39
4	30	4	41	71
5	34	5	31	65
6	28	6	14	42
7	20	7	14	34
8	10	8	6	16
9	13	9	7	20
10	2	10	6	8
11	1	11	4	5
12	..	12	3	3
13	2	13	..	2
14	1	14	..	1
17	1	17	..	1
22	1	22	..	1
	198		140	338

TABLE 2.—*Spiral Leaflets in the Valves of Heister*

	Cases															
Leaflets	1	2	3	4	5	6	7	8	9	10	11	12	13	14	17	22
Spirals																
1	..	..	..	7	6	11	7	4	6	2	1	..	1	...	...	...
2	..	..	..	3	4	6	3	5	8	4	2	3	...	...	...	...
3	..	..	..	..	1	1	..	..	..	..	..	..	1	1	...	1
4	..	..	..	..	..	..	..	..	..	..	..	..	...	...	1	...
Total spirals	..	..	..	10	11	18	10	9	14	6	3	3	2	1	1	1
Total cases	6	23	51	86	76	55	29	21	24	8	5	4	2	1	1	1
Spirals, percentage of total	..	..	..	11	14	32	33	42	58	75	60	75	100	100	100	100

dence of their previous existence, the leaflets varied from one to twenty-two in number. In eight instances in this normal group no leaflets were demonstrable grossly. This seems significant for it is not unusual to note the absence of leaflets in cases of cholelithiasis, as was noted in six of 123 cases. But their absence from specimens free from disease suggests that these ducts probably never possessed any valves. Terrier and Dally have likewise noted the absence of valves of Heister, but it is not

7. Brewer, G. E.: Preliminary Report on the Surgical Anatomy of the Gallbladder and Ducts from an Analysis of One Hundred Dissections, Ann. Surg. **29**: 721-730, 1899.

certain that previous disease did not exist in their cases. If one wishes to ascribe any functional purpose to these valves one must be able to correlate their absence in man and in the lower forms of life with that function.

I was unable to find any uniformity in the arrangement of the leaflets. In most specimens the leaflets ran in a spiral, clockwise manner, partially encircling the cystic duct and mortising between the leaflets on the opposite wall of the duct. In some instances the leaflets were not spiral (table 2), and in others they extended more than one-half to

Fig. 8.—Section of valve of Heister between walls of cystic duct (× 15).

three-quarters of the way around the duct, did not mortise into the space between the leaflets on the opposite side of the duct and frequently ran in a counterclockwise manner. In a particularly interesting specimen, having seventeen leaflets in the valves of Heister, I was able to demonstrate all of these variations. It seems significant that, in fourteen of the 338 normal gallbladder specimens, more than one leaflet ran in a counterclockwise manner.

From an anatomic point of view, therefore, it appears that the valves of Heister must be ineffectual in completely obstructing the flow of bile in either direction in the cystic duct. Moreover, whatever their function in the biliary system, it cannot be an essential one, as in eight instances no valves were present although the gallbladder was presumably normal.

HISTOLOGY

The valves of Heister are essentially projections of the mucosa at the outlet of the gallbladder arranged in a valvular manner. The epithelium is of the same tall columnar type, arranged in rugae of delicate branching forms, identical with those comprising the gallbladder mucosa. The mucosa of the cystic duct is similar to that of the gallbladder and the common duct, less intricate than the former and more

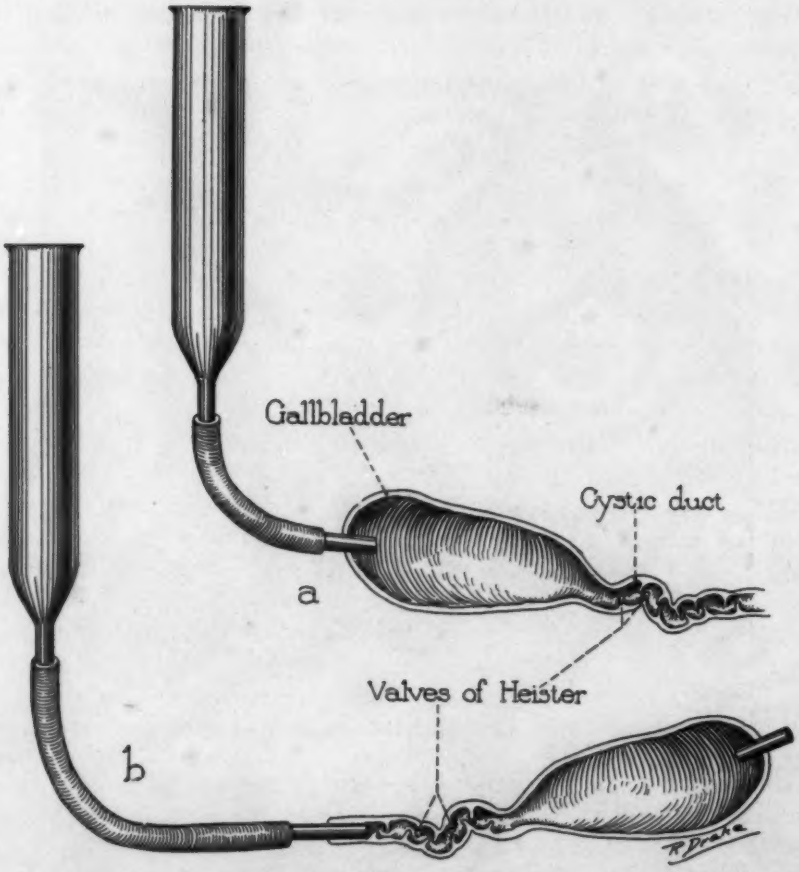


Fig. 9.—*A*, passage of fluid proximally; *b*, passage of fluid distally through cystic duct.

delicate than the latter. Its structure suggests a functional activity similar to that of the gallbladder; indeed, it is not difficult to believe that the mucosa of the cystic duct may be able to absorb fluids and probably lipoids almost as readily as the mucosa of the gallbladder comparable to that previously demonstrated.[8]

8. Mentzer, S. H.: Cholesterosis of the Gallbladder, Am. J. Path. **1**:383-388 (July) 1925.

The cystic duct is composed of smooth muscle fibers running in three directions, in a manner comparable to that in the wall of the gallbladder. The musculature of the valves of Heister has been the subject of considerable study, and some authors doubt the presence of longitudinal fibers in the leaflets. These, however, may be seen in any freshly prepared specimen on serial section (fig. 7). The circular smooth muscle fibers constitute the bulk of muscle in the leaflets themselves, and are, apparently, a continuation of the circular fibers of the cystic duct (fig. 8). I have not been able to demonstrate any sphincter arrangement of circular fibers at the terminal end of the cystic duct. Indeed, the duct was patent in all of the specimens, and a probe could be easily passed through it; it is not until the probe reaches the first leaflets that obstruction is met with.

The subserosal fat layer is relatively thick, as it is in the wall of the gallbladder. The serosal layer is thin and composed of squamous cells.

PHYSIOLOGY

Heister believed that the valves were placed in the cystic duct for the purpose of storing bile in the gallbladder until such time as the body needed it. This anthropomorphic view is held even now; it is, in fact, part of the accepted theory of the function of the gallbladder. Lyon's [9] application of Meltzer's law of contrary innervation of the gallbladder explained the opening of the valves of Heister to permit the passage of bile into the common duct. Schmieden [2] believes that the valves had something to do with the emptying of the gallbladder. Haberland,[10] Winkelstein and Aschner [11] believe the respiratory squeeze is sufficient to express bile from the gallbladder and past the valves of Heister into the common duct. Barker,[12] in 1907, expressed the belief in a unique function of the valves; namely, that the gallbladder secreted mucus at the rate of about two ounces a day but that this secretion was too viscid to pass down the cystic duct and, therefore, when the body needed the secretion the valves of Heister opened to permit bile to enter the gallbladder from the hepatic ducts, to dilute the viscous secretion, so that it could pass readily down the cystic duct. When the gallbladder secretion was no longer needed by the body the valves would close. He stated that there are ten of these valves to effect such closure.

---

9. Lyon, B. B. V.: Diagnosis and Treatment of Diseases of the Gallbladder and Biliary Ducts, J. A. M. A. **73**:980-982 (Sept. 27) 1919.

10. Haberland, H. F. O.: Studien an den Gallenwegen, III, Die Funktion der Gallenblase, Arch. f. klin. Chir. **130**:625-646, 1924.

11. Winkelstein, A., and Aschner, P. W.: Experimental Studies on Entrance of Bile Into Duodenum, Am. J. M. Sc. **169**:679-686 (May) 1925.

12. Barker, M. R.: What Is the Function of the Gallbladder? And Why the Folds of Heister in the Cystic Duct? Med. Rec. **72**:555-558, 1907.

Sweet,[13] in 1924, suggested that the valves of Heister prevented the egress of bile from the gallbladder, that bile once in the gallbladder never left it by way of the cystic duct. As my anatomic studies did not help me to understand either of these contrary views, I undertook the following experimental study.

Twenty-two normal gallbladders with their attached cystic and common ducts were tested for the patency of their cystic ducts. One end of the common duct was ligated; to the other end was fastened a pipet whose smallest bore measured 3 mm. (the size of a small cystic duct). The pipet was connected with a measuring funnel and the latter filled with 25 cc. of glucose solution of varying strengths. The funnel was raised 30 cm. above the level of the gallbladder so that gravity flow forced the solution through the cystic duct and into the gallbladder (fig. 9). The time required for the passage was noted in each instance. In none of the twenty-two specimens was there complete obstruction to the

TABLE 3.—*Time Required for Passage of Glucose Solutions Through the Cystic Duct, Minutes*

Glucose solution, 85 per cent	In	5	4	9	3	11	4	8	13	10	5	7	14	8	17	10	6	15	9	7	12	6	8	
	Out	4.5	5	7.5	4	10	6	7	14	11	7	5	12	7	15	8	6	13	11	6	13	5	9	
Glucose solution, 50 per cent	In	3	3	6	2	8	3	6	10	7	4	5	10	6	12	7	4	11	6	4	8	5	5.5	
	Out	3.5	4	5	3	7	5	5.5	11	8	5.5	4	7.5	5	9	5	3.5	8	7	4	9	4	5	
Glucose solution, 110 per cent	In	8	6	12	5	14	6.5	11	16	14.5	8	10	17	11	21	14	8	18	12	10	15	7	11	
	Out	7	7	10	6	12	8	8.5	18	15	8.5	7	16	10	18	11	7	16	14	9	13	9	12	

flow of the solutions. The time required for the passage varied, from three minutes in one instance to seventeen in another (table 3). Obviously, the number of leaflets comprising the valves of Heister, the diameter of the cystic duct and its tortuosity were the determining factors in the time element. Solutions of approximately one-half and twice the viscosity of normal bile were then used, and in every instance they passed through the cystic duct.

Similar experiments were conducted on the same twenty-two specimens to determine the patency of the cystic duct in the opposite direction. The apparatus was connected with the fundus of the gallbladder so that solutions passed through the cystic duct into the common duct (fig. 9). The conditions for the experiments were identical except for the reversal of the direction of flow of the fluids. In this series also, there was no instance of obstruction to the flow of the glucose solutions, and there was no material change in the rate of flow of identical solutions in either direction through the cystic duct (table 3). In one instance it required five minutes for 25 cc. of the glucose solution of "normal" viscosity to

13. Sweet, J. E.: The Gallbladder: Its Past, Present and Future, Internat. Clin. **1**:187-226 (March) 1924.

pass through the cystic duct from the common duct end, whereas seven minutes were consumed in passing in the opposite direction. But in five instances when glucose of like viscosity was used, less time was required for the passage from the gallbladder into the common duct compared to that in the opposite direction (table 3). In the remaining sixteen cases the rate of passage was essentially the same in either direction. Therefore, it was not possible to show any material change in the rate of flow of solutions in opposite directions through the cystic duct.

These experiments were handicapped from two standpoints, and therefore the data obtained are of suggestive value only. First, the specimens were obtained at necropsy, none later than eight hours after death. However, muscle tonus was gone. In vivo, muscle tone must play a part in the activity of the valves, even though it is slight. Second, the work is subject to error consequent on removal of the specimen ex situ. The cystic kink, although present in only a small proportion of the series (5 per cent), is altered in the operative manipulation.

Verification of the experiment might be made on the intact dog but this would not be wholly satisfactory since the dog's valves have but few and small leaflets.

PATHOLOGY

That the leaflets of the valves of Heister are concerned in disease of the gallbladder is obvious in any study of cholelithiasis. In seven of a series of 612 postmortem examinations inspissated bile was found packed in the leaflets and gallstones were found in seventeen. Such obstructions play a part in hydrops and probably in many cases of empyema of the gallbladder. Inspissated bile alone, when packed in the leaflets of the cystic duct, may produce sufficient obstruction to check the flow of bile from the gallbladder; thus the bile becomes excessively concentrated with probable change in the relative content of bile salt. In such event a change in the acidity of the bile would occur, and, according to Lichtwitz's [14] theory of the formation of gallstones, the ideal conditions for biliary calculi would be present.

Naunyn [15] has emphasized the part stasis of bile plays in the formation of gallstones, as produced by mechanical obstruction from kinking of the cystic duct, or by actual blockage of the duct itself. Schmieden believes that kinking of the duct alone, without inflammatory or obstructive changes, is sufficient to cause severe colic in the area of the gallbladder.

---

14. Lichtwitz, L.: Experimentelle Untersuchungen über die Bildung von Niederschlägen in der Galle, Deutsches Arch. f. klin. Med. **92**:100-108, 1907.

15. Naunyn, B.: Zur Lehre vom Aufbau und Umbau der Gallensteine, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **37**:545-550, 1924.

CONCLUSIONS

1. There are two contrary views with regard to the function of the valves of Heister; they are (*a*) that the valves aid in the storage of bile in the gallbladder until digestive demands require its egress from the gallbladder, and (*b*) that once bile has entered the gallbladder the valves prevent it from leaving by way of the cystic duct. Anatomic study of the valves does not favor either hypothesis.

2. A study of necropsy specimens showed that solutions passed in either direction through the cystic duct with equal facility.

3. The functional activities of the valves of Heister cannot be very important, since the majority of animals do not possess the valves or their functional equivalent. Moreover, eight normal gallbladder specimens from human beings examined at necropsy were without leaflets or indications of their having existed.

4. The study suggests that the valves of Heister check the rapid passage of bile into or out of the gallbladder, presumably so that bile in the gallbladder may remain at a relatively uniform consistency. If such is the function of the valves they aid in maintaining the gallbladder as a uniform sampling organ of bile, as suggested by Mann.[16]

16. Mann, F. C.: The Functions of the Gallbladder, Physiol. Rev. **4**:251-273 (April) 1924.

BRITTLE BONES AND BLUE SCLERA

HEREDITARY HYPOPLASIA OF THE MESENCHYME *

J. ALBERT KEY, M.D.

ST. LOUIS

1. INTRODUCTION

Having had under treatment a typical case of that type of fragilitas ossium which is commonly called "brittle bones and blue sclera," I am in a position to describe for the first time the pathology of the condition, and to add certain clinical observations to those which are included in the rather extensive literature on the subject.

The term "fragilitas ossium" is loosely applied to conditions that are characterized by an abnormal fragility of the bones. Bone fragility may be congenital or acquired, and may be due to developmental defects or to local or general absorption of the mineral constituents of normal bone. It is one of the most obscure subjects in modern medicine. The terminology is confused and the pathology is not well understood.

Our knowledge is particularly vague in regard to the so-called idiopathic or developmental types of bone fragility. This includes three fairly well defined clinical conditions: (1) osteopsathyrosis, described by Lobstein in 1833 as a definite clinical entity; (2) osteogenesis imperfecta, described by Vrolik in 1849 as a separate condition, and (3) the syndrome of brittle bones and blue sclera, described by Spurway [1] in 1894.

Hundreds of articles have been written on fragilitas ossium in general and the foregoing conditions in particular, but it is still a question whether or not they are all merely different terms for one condition. In regard to osteogenesis imperfecta and idiopathic osteopsathyrosis, Looser [2] prefers to call them osteopsathyrosis congenita and tarda, holding that in each the pathologic process is the same, the only difference being that in the former the fractures are present at birth while in the latter the fractures occur in infancy or childhood. Somewhat similar views are held by Sumita,[3] Bauer [4] and others who have recently studied the pathology of the first two types of fragilitas ossium.

---

* From the Shriners' Hospital for Crippled Children, and the Department of Surgery, Washington University School of Medicine.

1. Spurway, J.: Hereditary Tendency to Fracture, Brit. M. J. **2**:845, 1896.

2. Looser, E.: Zur Kenntniss der Osteogenesis Imperfecta congenita et tarda, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **15**:161, 1906.

3. Sumita, M.: Beitrage zur Lehre von der Chondrodystrophia foetalis und Osteogenesis imperfecta, Deutsche Ztschr. f. Chir. **107**:1, 1910.

4. Bauer, K. H.: Ueber Identität und Wesen der Sogenannten Osteopsathyrosis und Osteogenesis imperfecta, Deutsche Ztschr. f. Chir. **160**:289, 1920.

In regard to the third type which is associated with blue sclera, the pathology is largely unknown as Bronson's [5] description of the structure of the sclerotic coat of an eye from a case of brittle bones and blue sclera is the only report on the pathology of any of the tissues which I have been able to find in the literature. Not only is the pathology unknown but descriptions of the various clinical aspects of the condition are scattered through a rather extensive literature and it is only with difficulty that one is able to obtain a comprehensive clinical picture of the syndrome.

In our case we have roentgenograms of the entire skeleton and microscopic sections of the bone, tendon, muscle and skin from material removed at operation. We have determined the basal metabolism, studied the blood chemistry, and have also obtained the total phosphorus, calcium and nitrogen balance over two six day periods. The chemical analyses are being made by Dr. Ethel Ronzoni and will be reported in a later article.

From our own observations and an analysis of the cases reported in the literature we are able to describe a clear cut clinical syndrome which we shall term hereditary hypoplasia of the mesenchyme. The most prominent feature of the condition is that the sclerae of the affected persons appear to be china blue in color and that the blue sclerae are transmitted as a dominant hereditary characteristic. Many of the affected persons are afflicted with fragilitas ossium, hereditary deafness and hypermotility of the joints. All of the abnormalities seem to be due to defects in the development of some of the tissues which arise from the mesenchyme.

In this article we are not especially concerned with the possible identity of the various types of fragilitas ossium, but shall endeavor to give as completely as our present knowledge permits the clinical and pathologic picture of the condition which we call hereditary hypoplasia of the mesenchyme. As the condition is a very complex one it seems best to consider it under the following headings: history, report of case, heredity, physical characteristics, the eyes, deafness, fractures, deformities, conditions of the joints and muscles, roentgenographic appearance of the bones, pathology, other abnormalities, laboratory findings, comment and summary.

2. HISTORY

Blue sclera was first described by Von Ammon in 1839. Credit for the first recognition of the association of brittleness of the bones and a blue appearance of the sclera is universally given to Eddowes,[6] who in a brief note in the *British Medical Journal* in 1900 reported three

5. Bronson, E.: Fragilitas Ossium, Edinburgh M. J. **18**:240 (April) 1917.

6. Eddowes, A.: Dark Sclerotics and Fragilitas Ossium, Brit. M. J. **2**:222, 1900.

cases. I find, however, that the claim to priority by Spurway [7] is justified. In the *British Medical Journal* in 1896, Spurway [1] described a family of fourteen persons in four generations; ten of these had had multiple fractures, and he noted that the only other abnormality common to many members of the family was a curious bluish tinge of the eyeball which in some members was very marked.

The publication of Spurway's findings apparently attracted little attention as the article has not been mentioned in any of the succeeding articles on the subject. In 1900 Eddowes in a short note called attention to the syndrome, and in 1908 Peters [8] reported a family in which blue sclera was transmitted through four generations.

Since 1910 the syndrome has been widely studied, its hereditary nature has been established, and certain other conditions have been added to the original symptom complex of blue sclera and brittle bones. Chief among these is hereditary deafness, the occurrence of which was noted independently in 1917 by van der Hoeve and de Kleijn [9] and by Bronson.[5]

3. REPORT OF CASE

History.—A girl, aged 12 years, was admitted complaining that her bones were easily broken, having had thirty-three fractures.

The father was living and well, and the father's family history was negative. The mother was living and in good general health. She had blue sclera, was deaf, and had had two fractures. The grandmother and the great-grandmother on the mother's side of the family had blue sclera and were deaf. It is not known whether or not they had fractures. The patient had three brothers and two sisters. All were living, and all had blue sclera. Two brothers and one sister had had multiple fractures.

The mother was a rather large woman, with a height of 66 inches (167.6 cm.) and weighing 184 pounds (83.5 Kg.). The maternal grandmother was of small stature.

The patient had been a normal full-term baby, had nursed six months, and had then fed on condensed milk. She began to walk at about 18 months. Her dentition was normal. In her second year she was severely ill with infantile diarrhea. There had been no illness since, except an occasional cold. She has had none of the exanthemas. Menstruation began at 12 years and was normal and regular.

Present Illness.—The first fracture occurred in her third year when she slipped and fell to the floor, breaking the right forearm. At the age of 3 she fell and broke her right leg. The leg was broken again the next year and healed in a position of deformity, and has not been straight since, though it was fractured several times manually, and at one time a wedge of bone was removed in an attempt to straighten it. She fractured the left femur once, both legs and both forearms

---

7. Spurway, J.: Fragilitas Ossium, Blue Sclerotics and Otosclerosis, Brit. M. J. **1**:826, 1917.

8. Peters: Blaufärbung des Augapfels, Klin. Monatsbl f. Augenh. **46**:130, 1908; Blaue Sclera und Knochenbrüschigkeit, ibid. **51**:524, 1913.

9. Van der Hoeve, J., and de Kleijn, A.: Blauwe Sclera, Nederl. Tijdschr. v. Geneesk. **1**:1003 (March 31) 1917; Blaue Sclera, Knochenbrüchigkeit und Schwerhörigkeit, Arch. f. Ophth. **95**:81, 1918.

several times, and both clavicles at least once. In all there had been thirty-three fractures. At the age of 6 she was given crutches and a brace for the right leg, but broke the left leg several times while wearing the brace on the right. During the period from 8 to 10 years she walked on her knees. During the last two years she had been confined to a wheel chair. The fractures had always occurred after very slight violence. The last one (the fracture of the right leg which at present was not united) occurred when she was walking on her knees and attempted to get up on the curb. Her leg struck the curb and the bone was broken. The fracture occasioned so little pain that she continued to the theater where she was going and sat through and enjoyed the performance. Her father stated that this lack of pain had been a characteristic feature of all her fractures.

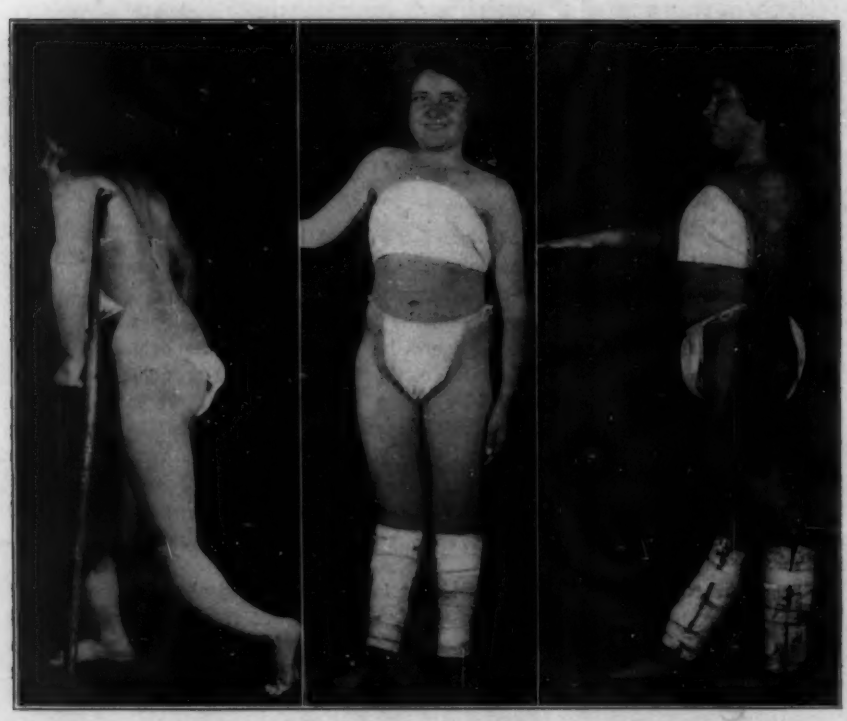


Fig. 1.—Patient with hereditary hypoplasia of the mesenchyme before and after correction of the deformities.

As an example he cited an instance when her physician was examining her left forearm eight weeks after a fracture: in testing for the firmness of union, the bone was heard to snap as it was broken again. But the patient "didn't bat an eye," and complained of little pain.

Physical Examination.—The patient was a rather obese young girl, with a height of 55.5 inches and weighing 101 pounds (45.8 Kg.). She was rather short and was unable to walk or stand without support (fig. 1). The skin was fair, rather dry and delicate in texture, and was covered with freckles. The hair of the head was abundant and brownish red. It was dry and coarse. The

eyebrows and eyelashes were normal. The axillary hair and pubic hair were normal. The nails were normal.

Head: The head was normal in contour, with a circumference of 19½ inches (49.4 cm.). The ears were rather small. There was some retraction of the ear-drums. The hearing was normal.

Fig. 2.—Passive and active hyperextension of the fingers, deformity of right elbow and freckles on arms.

Nose: The septum was slightly thickened, and both middle turbinates were slightly enlarged.

Eyes: The pupils were equal and regular. They reacted normally to light and accommodation. The ophthalmoscopic examination was negative. The extra-ocular movements were normal. Intra-ocular tension was normal. The sclera appeared to be a clear china blue in color. The blue tint was deeper in the

anterior part of the bulb in a zone around the cornea corresponding to the uvea. There was a slight embryotoxin.

Throat: The tonsils had been removed. There were some remnants of adenoid tissue present. The tongue was normal. The teeth were all present and in unusually good condition. They were normal in size and structure and in good alinement. There was one small cavity which was filled.

Glands: There was no glandular enlargement; the thyroid was not enlarged; the breasts were normal.

Chest: The chest was rather full and barrel shaped. The costal angle was about 90 degrees. Expansion was good and the lungs were normal.

Fig. 3.—Hyperextension of the knee and range of motion in the ankles.

Heart: The heart was normal. The pulse was 80; the systolic blood pressure was 120, the diastolic 80. The arteries were soft. The abdomen was normal.

The external genitalia were normal. The musculature was normal except in the lower extremities, where there was some atrophy and weakness from disuse.

The reflexes were normal. Intelligence was normal. The spine was lordotic but otherwise normal.

Upper Extremities: The shoulders were normal. There were slight deformities of both elbows, the carrying angle being lost and the inner condyle of the humerus being higher than usual. Flexion of the elbows was normal. Extension was limited to 180 degrees on the right and 170 degrees on the left. Supination of the right forearm was limited. The fingers were slender and tapering. Movements of the wrists and fingers were more free than normal. It was possible to hyperextend the fingers to about 90 degrees (fig. 2).

Lower Extremities: The length of the right leg was 30 inches (76.2 cm.); of the left, 29¼ inches (74.2 cm.). The length of the right femur was 17 inches (42.5 cm.); of the left, 16¾ inches (42.4 cm.). The circumference of the right thigh was 16 inches (40.6 cm.); of the left, 15½ inches (38.7 cm.). The circumference of the right calf was 9¼ inches (23.4 cm.); of the left, 10¼ inches

Fig. 4.—Sclerosis and deformity of the right tibia and fibula; the arrow points to a subperiosteal fracture due to a slight injury.

(26 cm.). The thighs were normal. The patellae were unusually small. There was a marked anterior bowing of the right leg; the apex of the curve was in the lower half of the leg and was covered by an extensive scar which was adherent to the bone. In this scar was a small ulcer. The curve described an arc of 70 degrees, and was chiefly in the lower half of the leg, the upper half of the leg being straight (fig. 4). On the left side there was an anterior bowing in the

upper third of the leg, the lower part of the leg being straight. The angle of the deformity was 60 degrees. There appeared to be an incompletely united fracture of the tibia at the apex of the deformity (fig. 5). The feet were relaxed and pronated. There was hypermotility of all the joints of the lower extremities (fig. 3).

Ankles: Flexion was to 50 degrees and extension to 150 degrees.

Fig. 5.—Sclerosis and nonunion of the left tibia.

Knees: There was increased lateral mobility and hyperextension on the right to 22 degrees, and on the left to 15 degrees. With the knee extended it was possible for the patient to flex the hip to such a degree that the heel could be placed over the shoulder and behind the head.

Urinalysis: The urine was consistently normal.

Blood: Hemoglobin was 85 per cent; red blood cells totaled 5,432,000; white blood cells, 10,500.

Differential Count: Polymorphonuclears totaled 51 per cent; polymorphonuclear eosinophils, 3 per cent; lymphocytes, 34 per cent, and monocytes, 12 per cent.

Basal Metabolism: The finding was —3, normal. The tuberculin, Wassermann and Schick tests were negative.

Blood Chemistry: The p_H was 7.58; phosphates totaled 4.06 mg. per hundred cubic centimeters, and calcium, 12.17 mg. per hundred cubic centimeters.

The roentgenographic findings are given in section 11.

Operations.—An operation was performed on the left leg by Dr. G. C. Abbott, Jan. 5, 1925. An incision was made over the internal aspect of the junction of the upper and middle thirds of the tibia where there was a pronounced angulation forward. A pseudo-arthrosis was found with massive sclerotic bone in the posterior half of the upper end of the lower fragment, and with a slight amount of sclerotic bone in the upper fragment. The bone was sectioned obliquely with removal of wedges from both fragments, one from the posterior aspect of the lower fragment and a second from the anterior end of the upper fragment. The fragments were then overlapped and fixed with two beef bone screws. It was not necessary to do an osteotomy of the fibula. A general anterior curvature of the tibia that could hardly be corrected remained, but the main deformity was greatly improved. The wound was closed with catgut to the periosteum, silk to skin. The leg was fixed in a plaster-of-paris cast. The step operation for the cure of the nonunion in the fracture of the upper third of the tibia is shown in figure 6.

February 15, convalescence was uneventful. The stitches were removed. The wound was clean.

February 18, the plaster was changed. Clinically the leg felt solid.

February 25, the patient while in a wheel chair struck her right leg against a bed. There was no swelling, ecchymosis or false motion, but there was slight tenderness over the lower third of the right tibia and the roentgen ray showed an incomplete fracture of the tibia at this point (fig. 4).

March 2, I performed an operation on the right leg. The rather extensive scar over the anterior surface of the apex of the curve in the tibia was excised by an elliptical incision about 5 inches (12.7 cm.) long. The scar was intimately bound to the periosteum, which was very thin and delicate, and was stripped from the bone with ease. The tibia was then exposed by stripping back the periosteum in the area of the curve, and with an osteotome a wedge with an anterior base was removed. The bone was very hard and brittle. The fibula was exposed through a lateral incision. In making this incision it was found that the fibula lay very deep in the leg and posterior to the tibia. There was a thick layer of superficial fat, and the fascia of the leg was not white and glistening as is normal but was a delicate pink connective tissue membrane. The fibula was divided with an osteotome. An attempt was made to correct the deformity, but shortening of the soft tissue on the posterior surface of the leg interfered with correction. A curved incision about 5 inches long was made on the posterolateral surface of the leg, and the tendon of achilles was exposed. The tendon of achilles was most unusual in that it was about the diameter of a lead pencil (one-fourth inch, or 0.6 cm.) and translucent in appearance, there being a striking absence of the dense white fibrous tissue usually seen. Its color was a delicate pink rather than white. The tendon of achilles was split longitudinally and sectioned by the Z method and lengthened about 2½ inches (6.2 cm.). The wound was then closed and an attempt was made to straighten the leg. There was

considerable difficulty in accomplishing this and the ends of the cut tibia were remodeled with the rongeur forceps so that the lower fragment was pointed on the upper end, and the lower end of the upper fragment hollowed out to form a socket into which the lower fragment fitted. It was then possible completely to correct the deformity; but, with this done it was found that the skin edges could

Fig. 6.—Left tibia eleven weeks after operation showing callus formation and beef bone screws in place.

not be made to close over the denuded bone. Consequently, a tension cut about 5 inches long was made through the skin on the lateral surface of the leg, and tension sutures of silk and catgut were used to draw the skin together. After this was placed, the tension sutures were removed. The tension incision was left open and covered with petrolatum gauze. The leg was encased in plaster with the deformity partly corrected.

In addition to the striking delicate pink color of the tendon of achilles and of the deep fascia as noted in this patient, there was an unusual friability of the soft tissues. The blood vessels tore easily. The periosteum was so delicate that it could be pulled apart with a pair of tissue forceps, and the scar over the tibia was much less dense than normal scar tissue. This condition of the fibrous

Fig. 7.—Right leg two weeks after osteotomy showing callus formation.

tissue was in sharp contrast to that of the bone which seemed to be unusually hard and brittle.

March 12, the stitches were removed. The wounds were clean.

April 2, the cast was changed. The union was firm. The deformity in the lower third of the leg below the site of the operation was still present.

April 20, osteoclasis of the right leg was performed by Dr. Key. With the osteoclast the bone was fractured at the apex of the forward bow. The

bone was fractured with little force. The tender skin over the bone was lacerated by the pressure. This was dressed with picric acid and the leg was put up in plaster in the corrected position.

April 30, convalescence was uneventful; the abrasion was almost healed.

Fig. 8.—Right leg twelve weeks after osteotomy and eight weeks after osteoclasis below, showing callus formation and incomplete correction of the deformity.

May 20, the cast was changed. The union was firm. The deformity was not completely corrected, but on account of the marked genu recurvatum it was felt advisable not to correct fully the anterior bow of the lower leg (fig. 8).

June 10, the patient was learning to walk with short plasters around the legs (fig. 1).

June 30, the patient was discharged, walking with crutches, and was told to wear celluloid splints on the legs.

4. HEREDITY

It is to be emphasized that the factor of heredity is of fundamental importance in the condition with which we are dealing. Fragile bones or blue sclera occurring singly or together in a patient with no similar cases in the family cannot be considered as belonging to the group under discussion.

That the condition is hereditary was pointed out by Spurway [1] and Peters [8] in their early articles.

During the last fifteen years many family trees have been published which show that blue sclera and brittle bones are dominant hereditary characteristics in certain families. The most important of these are summarized in the accompanying table. The families of Voorhoeve [10] and Bolten [11] are not included in the table because they are not typical.

Summary of the Reported Families with Hereditary Hypoplasia of the Mesenchyme

Year	Author	Number in Family	Number of Susceptible Persons	Number Affected	Number with Fracture	Deafness	Transmitted by Male	Transmitted by Female	Generations	Affected Males	Affected Females
1896	Spurway [1]	14	13	10	10	?	3	0	4	6	4
1908	Peters [8]	10	10	9	3	?	2	2	4	5	4
1910	Stephenson [18] and Harman [16]	55	52	31	?	?	1	10	5	12	19
1911	Burrows *	29	21	13	9	?	1	4	4	5	8
1911	Rolleston †	6	6	4	1	?	0	2	3	1	3
1912	Adair-Dighton [22]	12	12	9	5	1	2	1	4	6	3
1913	Conlon [23]	27	22	18	6	..	2	4	5	7	11
1914	Cockayne [17]	16	16	6	6	?	0	3	4	3	3
1915	Conrad and Davenport [12]	42	37	22	22	?	1	5	4	11	11
1917	Van der Hoeve and de Kleijn [9]	22	17	10	10	11	0	3	4	2	9
		6	6	6	5	3	2	0	3	5	1
1917	Bronson [5]	55	33	21	13	7	1	7	4	8	13
		8	8	7	4	0	2	1	3	2	5
1919	Hass [20]	24	14	8	8	7	2	2	3	6	2
1921	Blegvad and Haxthausen [41]	23	21	10	8	3	1	2	3	2	8
1921	Freytag [25]	18	17	11	11	9	2	3	5	6	5
1922	Alexander ‡	6	6	6	4	1	0	3	4	0	6
1922	Stewart §	19	19	8	4	1	0	2	2	2	6
1923	Straat [24]	10	10	6	5	3	0	2	3	3	3
1923	Stobie [24]	66	39	18	8	8	4	4	5	8	10
1926	Key	9	9	7	4	3	0	3	3	2	5
	Totals	477	388	241	146	56	26	63	..	102	139

* Burrows, H.: Blue Sclerotics and Brittle Bones, Brit. M. J. **2**: 16, 1911.

† Rolleston, J. D.: Inherited Syphilis and Blue Sclerotics, Proc. Roy. Soc. Med. **4**: 96, 1910-1911; Ophthalmoscope **9**: 321, 1911.

‡ Alexander, J. B.: Fragilitas Osseum Associated with Blue Sclerotics in Four Generations, Brit. M. J. **1**: 677 (April 29) 1922.

§ Stewart, H.: Fragilitas Ossium Associated with Blue Sclerotics, Brit. M. J. **2**: 498 (Sept. 16) 1922.

The only study of the hereditary factor in fragility of bones which I found is that of Conard and Davenport.[12] They were able to find thirty-five families in the literature in which two or more cases of fragile bones occurred. Only the last four families of the series belong to our

10. Voorhoeve, N.: Blue Sclerotics, Lancet **2**:740, 1919.

11. Bolten, H.: Blauwe Sclerae, Nederl. Tijdschr. v. Geneesk. **2**:1747, 1923.

12. Conard, H. S., and Davenport, C. B.: Hereditary Fragility of Bone, Eugenics Record Office Bull. 14, 1915, Cold Spring Harbor, N. Y.

group of blue sclera and brittle bones. They concluded that the factor that determines the imperfect, brittle development of the bones is a dominant one and that "a parent who is, or who was in early life, osteopsathyrotic will have half of his children so affected no matter whom he marries except that, if the consort be also osteopsathyrotic, it is to be expected that three-fourths of the children will be affected."

Unfortunately the authors did not distinguish between the three clinical types of fragilitas ossium. In their family 10 the second generation seems to have osteogenesis imperfecta and these children were all born of healthy parents. The others of the first thirty families seem to be cases of osteopsathyrosis idiopathica. In these the condition was transmitted by the father thirty-one times, and by the mother only four times.

In the cases of brittle bones and blue sclera the condition is more often transmitted by the mother to her children, though it may be transmitted by either the male or the female, and in certain families, such as Spurway's [1] and van der Hoeve's and de Kleijn's [13] family Y, it was transmitted only by the male (table). In these families, there were no children born to affected females.

The characteristic feature of the heredity of blue sclera and brittle bones is that the condition is transmitted only by affected parents to their children. A generation is never skipped as is the case in hemophilia (knight's move of Bateson).

Children with normal sclera born of affected parents will have normal children. Furthermore, only the persons affected with blue sclera are subject to brittle bones and the other stigmas of the condition. The members with white sclera are also normal in other respects.

As was pointed out by Ruttin [14] the fractures occur in childhood while the deafness comes on in adult life. That is one reason why so few cases of deafness are recorded in the accompanying table. The other reason is that it was not described as a part of the syndrome until 1917 and in most of the families reported deafness has not been looked for.

In the third column of the table is given the number of susceptible persons. A susceptible subject is a person one of whose parents was affected with the hereditary type of blue sclera. In the twenty-one families there were 388 susceptible persons. Of these 241, or 62 per cent, inherited the condition of hypoplasia of the mesenchyme.

In considering the incidence of multiple fractures the family of Stephenson and Harman will be omitted as the presence or absence of

13. De Kleijn (footnote 9, second reference).

14. Ruttin: Ohrbefund bei Osteopsathyrosis, Monatschr. f. Ohrenh. **54**:305, 1919.

fractures was not noted. This leaves us 336 susceptible individuals and 210 affected individuals. Among these there were 146 cases of multiple fractures, an incidence of 42.5 per cent in the susceptible individuals and of 70 per cent in those who were affected with mesenchymal hypoplasia.

5. PHYSICAL CHARACTERISTICS

That persons who have blue sclera and brittle bones tend to be smaller in stature than normal was noted in 1910 in the family described by Stephenson [15] and Harmon.[16] In Cockayne's [17] family the affected members were all abnormally thin and light, two of the men weighing only about 90 pounds (40.8 Kg.) each while the unaffected members were of normal stature.

The affected members of Bronson's [5] first family spoke of themselves as being small boned in contrast to their relatives who had white sclera. Of those examined all but two were below the average height, and the affected children were from 1 to 2 inches (2.5 to 5 cm.) less in height than the average for their age.

Singer [18] described his patient as being small, slender and of the infantile type. The woman reported by Weichmann and Pool [19] was small and slender (height 1.4 meters, weight 35.5 Kg.). She had been of normal size as a child but had ceased to grow when she was 16 years old. Hass,[20] Blencke [21] and others have commented on the small stature in their cases. Our patient is 55½ inches tall. The normal height for a girl twelve years old is given by Holt [22] as 57.1 inches. Her weight after admission was 101 pounds (45.8 Kg.). This is about 21 pounds (9.5 Kg.) overweight, according to Holt's figures. As stated she was rather obese. Her mother, who had blue sclera was a rather large woman, but the other affected members of the family were of small stature.

---

15. Stephenson, S.: A Peculiar Appearance of the Eyes, Ophthalmoscope **8**: 330, 1910.

16. Harman, N. B.: A Pedigree of Five Generations of Blue Sclerotics, Ophthalmoscope **8**:559, 1910.

17. Cockayne, E. A.: Hereditary Blue Sclerotics and Brittle Bones, Ophthalmoscope **12**:271, 1914.

18. Singer, S.: Ein Beitrage zur Frage der Kombination abnormer Knochenbrüchigkeit und blaue Skleren, Ztschr. f. klin. Med. **97**:43 (May) 1923.

19. Weichmann, E., and Pool, H.: Zur Klinik der sogenannten blauen Skleren, München. med. Wchnschr. **72**:213, 1925.

20. Hass, J.: Zur Kenntniss der Osteopsathyrosis idiopathica, Med. Klin. **15**: 1112, 1919.

21. Blencke, A.: Ueber das gemeinsame Vorkommen, Ztschr. f. orthop. Chir. **45**:406, 1924.

22. Holt and Howland: Diseases of Infancy and Childhood, New York, 1922, p. 23.

Scoliosis and kyphoscoliosis have been reported by van der Hoeve and de Kleijn [9] and others. The small stature is in many cases partly the result of the deformities but in others it is simply due to the fact that the bones are shorter and slenderer than normal.

Bronson [5] has called particular attention to the peculiar types of head found in the affected members of her two families. In the first family the frontal and occipital bones were unusually prominent yet there was none of the squareness of the rachitic head. The suture lines of the occipital bone were palpable and there was a history that two members of the family had had patent fontenelles throughout life. In the second family, the abnormality of the head was more pronounced. The characteristics of the head were "a frontal and supra-aural prominence, a slight tilting downward of the axis of the eye, ears bent outward and downward, and a slightly underhung jaw." This is a typical osteogenesis imperfecta type of skull.

In Ruttin's [14] case the skull was of the hydrocephalic type and the sella was cuplike. Stenvers [23] noted an unusual configuration of the hind part of the skull. The deformity was a rather definite angulation of the occiput as though it had been folded on a hinge, and there was a clear fracture or vessel line in this region. This is similar to the occipital prominence noted by Bronson in the Currie family. In our case the head was rather large, 19½ inches (49.4 cm.) in circumference, and there was a definite prominence of the forehead, but there was no unusual occipital bulge or angulation (fig. 1). We do not consider the shape of the head as abnormal, and this is also true of six other affected members of the family of whom we procured photographs. Buxton, who examined the Oxford family reported by Stobie,[24] concluded that the heads were not abnormal.

6. THE EYES

An abnormal blue appearance of the sclera is an essential part of the clinical picture. As stated in the section on heredity, only those members of the family who have blue sclera are subject to the abnormalities to be described. The color has been described as a clear china blue, a slate blue or a gray blue. The depth of the blue varies in different individuals of the same family, as was noted by Spurway.[1] The color is not uniform but is darker in the anterior portion of the sclera over the ciliary body. Behind the ciliary body, which as a rule can be distinctly outlined on the sclera in these eyes, the lighter gray blue extends as far back as the sclera can be seen.

---

23. Stenvers, H. W.: Röntgenologische Bemerkungen, Arch. f. Ophth. **95**:94, 1918.

24. Stobie, W.: The Association of Blue Sclerotics with Brittle Bones and Progressive Deafness, Quart. J. Med. **17**:274 (April) 1924.

All authorities are agreed that the blue of the sclera is not due to a pigmentation but is the result of an abnormal transparency of the sclerotic coat of the eye which permits the blue uvea to shine through. Eddowes [6] suggested that the transparency of the sclerotics indicated a want of quantity or quality of the fibrous tissue forming the framework of the various organs of the body and probably explained the want of spring or toughness in the bones of these persons.

Peters [8] believed the sclera to be actually thinner than normal. Conlon [25] was able to demonstrate the increased transparency by means of a Sach's lamp. He considered the unusual transparency as probably due to some change in the quality of the tissue rather than to an actual thinning of the sclera. In support of this view he stated that if the sclera were thinned one would expect to find cases of buphthalmos in these families, or at least of axial myopia.

Fridenberg, who examined Herrman's [26] case, stated that if the sclera were thin, some cases should show distention of the globe, as in infantile glaucoma or hydrophthalmos or coloboma or posterior staphyloma. He suggests that the blue sclerotic and lead gray iris are due to a transparency dependent on the absence of lime salts in the connective tissue of the sclera and iris.

In the two instances in which blue sclera were subjected to histologic examination exactly opposite conclusions were drawn. Buchanan [27] studied an eye removed from a girl aged 9 years who had blue sclera. The removal was necessitated by an injury to the eye. In this eye the cornea was three-fifths and the sclera was only one-third the normal thickness. There was a decrease in the number but no change in the size of the sclerotic fibers.

Bronson [5] reported the condition of the sclera of an infant aged 11 months who was a member of her first family and who had blue sclera. The eye was removed post mortem. J. V. Patterson examined the sections and stated that the sclera was of normal thickness and that the size and number of the fibers were normal for a child of that age. Bronson stated that Buchanan's case had no family history of fractures and that one has no reason to assume that it belongs to the fragilitas blue sclerotic group.

Embryotoxon was noted by Peters [8] in the family described by him. It is apparently not of great significance in the syndrome. It was present in the families reported by Stephenson,[15] Harman,[16] Conlon,[25]

---

25. Conlon, F. A.: Five Generations of Blue Sclerotics and Associated Osteoporosis, Boston M. & S. J. **169**:16, 1913.

26. Herrman, C.: Blue Sclerotics and Brittle Bones, Am. J. Dis. Child. **9**:203 (March) 1915.

27. Buchanan: A Case of Maldevelopment of the Cornea and Sclerotic, Tr. Ophth. Soc. **23**:267, 1903; Ophthalmoscope **8**:685, 1910.

and in the family Y of van der Hoeve and de Kleijn [9] but was absent in their family X. A slight embryotoxon was present in our case. Keratoconus was present in Behr's [28] case. Stephenson noted a Fuch's coloboma in his case. Cataract was present in two of the cases of van der Hoeve and de Kleijn. Most of the cases that were refracted showed astigmatism and hypermetropia (Conlon, Stephenson, Harmon, Bronson, van der Hoeve and de Kleijn and others). Myopia was noted five times by van der Hoeve but was not present in the other families described. The fundi were uniformly negative in all cases examined. The intraocular tension was normal.

It is to be noted that blue sclera occurs in other conditions, such as congenital buphthalmos, and when the whole development of the eye is backward. It may occur apparently spontaneously in persons normal in other respects, as in Bronson's Mrs. L. A slight blueness of the sclera may be present in anemia, tuberculosis and certain forms of heart disease.

On the other hand, there are a number of cases in the literature in which blue sclera and fragile bones occurred sporadically in persons in whose families there had been no similar cases: Bronson,[5] Herrman [26] Ostheimer,[29] Hoffmann,[30] Gutzeit [31] and others. Whether or not these cases belong in the group under discussion it is impossible to say. They certainly resemble our case in a great many ways. However, I have found no record to the effect that the disease has been transmitted to children in such a sporadic case.

7. DEAFNESS

The first mention of deafness in a case of mesenchyme hypoplasia was in 1912 by Adair-Dighton,[32] who simply noted its presence in a member of his family. Likewise Behr [28] in 1913 noted deafness in his case. The credit for definitely including hereditary deafness in the syndrome should be divided between van der Hoeve and de Kleijn [9] and Bronson,[5] who described the condition almost simultaneously in 1917.

Van der Hoeve and de Kleijn reported two families. In the first family all of the eleven patients with blue sclera who were examined were deaf. The deafness was of the otosclerotic type in all cases, but

28. Behr, C.: Beitrage zur Aetiologie des Keratoconus, Klin. Monatsbl. f. Augenh. **51**:281, 1913.

29. Ostheimer, M.: Fragilitas Ossium, J. A. M. A. **63**:1996, 1914.

30. Hoffmann, W.: Ueber Blaufärbung der Sklera und abnorme Knochenbrüchigkeit, Arch. f. klin. Chir. **107**:279, 1915.

31. Gutzeit, R.: Ueber blaue Sklera und Knochenbrüchigkeit, Klin. Monatsbl. f. Augenh. **68**:171, 1922.

32. Adair-Dighton, C. A.: Four Generations of Blue Sclerotics, Ophthalmoscope **10**:188, 1912.

in the advanced cases this was complicated by labyrinthine disease (nerve deafness). In the second family three of the six affected persons were deaf. They emphasize the fact that in many of the younger patients the beginning deafness had not been noticed but was brought out by the aural examination.

In Bronson's Currie family there were eight adults who had blue sclera and seven of these developed deafness in early adult life. The other adult died at the age of 23 and deafness had not been noted. Three of her patients were examined by J. S. Frazer. All showed otosclerosis and one also had nerve deafness. One adult of this family who had white sclera was examined and found to have normal hearing.

Four of Voorhoeve's [10] patients were examined for deafness and all showed labyrinthine deafness. Ruttin [14] gave a detailed examination of the deafness in his case and noted that the deafness develops in later life while the fractures occur in early life. Hass,[20] Straat,[33] Freytag,[34] Blenke [21] and Weichmann and Pool [19] noted deafness in varying degrees in their families. In the family of our patient the mother is deaf and so was the maternal grandmother. The family is widely scattered and it has not been possible to examine these or to get a detailed history of the other adult members of the family. Our patient is now 12 years old and her hearing is apparently normal, but it is probable that she will develop deafness in adult life.

To explain the deafness in her cases, Bronson assumes that there was a deposit of calcium salts in the middle ear. Stenvers,[23] in studying the skulls of the families of van der Hoeve and de Kleijn roentgenographically, found that the petrous bone cast a dense shadow and that there was a compact opaque mass covering and obscuring the entire vestibular region. From these findings he was able to make a clinical diagnosis of sclerosis and abnormal calcification of the labyrinthine system. Ruttin confirmed the presence of otosclerosis by histologic examination of the petrous bone.

8. FRACTURES

Multiple fractures are a characteristic feature of any series of cases of hereditary hypoplasia of the mesenchyme, though they are by no means present in every person affected with the blue sclera. In the 210 persons in the accompanying table who had blue sclera 146 had multiple fractures, an incidence of 70 per cent. It is to be emphasized that if one of the parents has blue sclera the children are liable to have brittle bones even though the parent had no fractures. The incidence of frac-

33. Straat, H. L.: Blauwe Sclerae, Fragilitas Ossium en Otosklerose, Nederl. Tijdschr. v. Geneesk. **1**:152 (Jan. 13) 1923.

34. Freytag: Ueber blaue Sklera u. Knochenbrüchigkeit, Klin. Monatsbl. f. Augenh. **66**:507, 1921.

tures in the children of parents with blue sclera is 42 per cent (table). In our family the mother has blue sclera but has had no broken bones. Four of the six children have had multiple fractures. The other two children are still quite young.

In contrast to osteogenesis imperfecta the fractures are not as a rule present at birth and are not spontaneous. In most cases they occur in early childhood and are always assignable to a definite cause, though the causative force is often less than would be necessary to break a normal bone. The fractures continue to occur off and on through childhood. In most instances the tendency of the bones to break easily decreases after puberty, and the average patient, if not crippled by deformities due to malunion of fractures received in childhood, is able to pursue a normal life. However, sometimes the brittleness of the bones persists into late adult life.

The number of fractures is not as a rule great. The average patient probably suffers from six to eight fractures, and it is unusual for any of these unfortunates to have more than ten. Our case with thirty-five fractures in a period of ten years is, with the exception of the case with sixty-one fractures reported by Terry,[35] the most severe that I have seen recorded. This is in sharp contrast to osteogenesis imperfecta, in which great numbers of fractures are the rule. Many of these children pass through a period of from one to two years when fractures are very frequent. In our case this period included the eighth and ninth years of life. During this time the patient hardly recovered from one injury before another occurred.

The long bones, especially those of the lower extremities, are the ones most frequently affected. In our case there were fractures of both clavicles, both arms, both forearms, one thigh and both legs. In the literature are instances of fractures of the mandible, ribs, patella, pelvis and fingers. The bones of the face, the scapula, the sternum and metacarpals, and the bones of the ankle and foot seem not to have suffered. There are no definite instances of fracture of the spine or skull, though the roentgenograms of Stenvers [23] are suggestive of old fractures in all of these regions.

In some cases certain bones seem to be especially brittle. European observers feel that the femur is fractured more frequently than any other bone. In our case the femur was broken only once, and the majority of the fractures occurred in the legs. Conard and Davenport [12] believe that the tendency to fracture certain bones is inherited, the weak bones varying in different families. The reports in the literature are too cursory to permit a checking up of this theory at present.

---

35. Terry, W. I.: Hereditary Osteopsathyrosis, Ann. Surg. **68**:231 (Aug.) 1918.

In regard to the character of the fractures, they are usually simple transverse or oblique breaks. Some of them are subperiosteal without displacement. Others are incomplete, being simply cracks in the bone (fig. 5). Greenstick fractures apparently do not occur and I know of no instance in which one of these fractures was comminuted. There is a history of a compound fracture of the right tibia in our case. It is the only one in the literature, I believe.

Reye [36] found most of the fractures occurring in the shafts of the long bones at the ends of the diaphysis near the epiphysis. In the other cases in the literature and in our family they have been limited to the diaphysis, but no particular region of the diaphysis has been favored. In this connection it is remarkable that there is no instance of a fracture of the neck of the femur in any of these families. The shafts of the bones are apparently so much weaker than the epiphyses that epiphyseal fractures do not occur. Likewise, there are no instances of epiphyseal separation among these cases.

The amount of pain and swelling occasioned by a fracture seems to vary in different cases. In our case they were relatively slight. This is contrary to the experience of Hass [20] and Blencke,[21] both of whom found a degree of pain in their cases commensurate with the fracture. The pain was, however, relieved by rest of the extremity. It is probable that the pain and damage to the soft parts vary inversely with the force exerted in producing the fracture. Their cases had relatively few fractures; our case had a great many. Any one who has seen acute fractures from slight violence to atrophic bones must have noticed that the pain and swelling are much less than occur in similar fractures caused by severe trauma to normal bones. In our patient the fractures were usually the result of slight force and were consequently accompanied by little damage to the soft parts and were not very painful.

Rapid healing of the fractures was noted by Spurway [1] in the first family reported. He stated that in one instance consolidation was quite firm at the end of four days. Hass [20] and Singer [18] report fairly firm union in from four to eight days. We discovered this to our chagrin in the treatment of our case. In the correction of the long curve in the right leg, the osteotomy corrected the upper part of the curve. The lower part was to have been corrected by an osteoclasis but the injury to the very tender skin necessitated a window in the cast for dressings. A forward bowing of the tibia occurred under the window and almost reproduced the original deformity. Twelve days after the operation we attempted to remold the limb manually, but the union was so firm that we were unable to do so. When the patient began to walk the marked

36. Reye: Ueber diffuse Blaufarbung der Sklera, Deutsche med. Wchnschr. 4:125, 1917.

genu recurvatum caused us to leave the slight anterior bow in the lower leg as her line of weight bearing seemed to be better than it would be if the bone were straightened.

The fractures tend to heal with a minimum amount of callus and deformity. This, I believe, is due to the fact that in many of the fractures there is little or no displacement and a minimum amount of damage to the soft parts and stripping up of the periosteum. In our case postoperative roentgen-ray examination showed about the normal amount of callus (figs. 6, 7 and 8). The nonunion of the left tibia in our case is, I believe, the only case of nonunion in this condition which has been reported (fig. 5). It was probably the result of inefficient fixation as the bone united promptly after operation. The nonunion of the patella reported by Gutzeit [31] occurred in a nonhereditary case.

Hass [20] noted that so firm is the union that refracture through the seat of an old fracture practically never occurs. This is probably true because the healing of a fracture in these cases is often accompanied by more or less sclerosis of the bone. In many instances the fractures heal perfectly and leave no sign even in the roentgenogram. However, in our case, in spite of the marked thickening of the cortex of the right tibia, it has been broken ten or twelve times in the lower half of the shaft (fig. 4).

9. DEFORMITIES

Many of these patients develop severe crippling deformities, especially of the lower extremities and spine. It is to be emphasized that these deformities are the result of malunion of fractures and are preventable. That they are not due to softening of the bones is illustrated by the necks of the femora and the contour of the pelvis in our case. Were the bones softened one would expect to find an osteomalacic type of pelvis and a bilateral coxa vara. On the contrary, the pelvis is normal in contour and there is a definite bilateral coxa valga (fig. 9). The coxa valga is probably a secondary change in the angle of the neck of the femur due to the fact that in this patient weight bearing has been considerably restricted since infancy. As will be mentioned below, the bones are unusually hard but brittle.

In our case, the shafts of the femora though slender are normal in contour. The deformities of the legs are clearly the result of old fractures. There is even less secondary curving in the bone above and below the deformity than one usually finds in such cases in growing children (figs. 4 and 5). The deformities of the forearms, elbows and clavicles are clearly the result of old fractures. The bones that have not been broken, though slender, are not bowed.

Scoliosis and kyphosis have been reported in several instances. Stenvers [23] noted that in those cases with kyphosis and scoliosis the deformities were sharp and angular such as result from mild crushing

fractures of one or more vertebral bodies rather than gradual curves, such as one would expect to find if the deformities were the result of general bone softening. Another possible explanation of these spinal curves is that they are due to the general laxity of the ligaments of the body. In our case the spine was lordotic and unusually flexible for such a short and heavy torso.

10. CONDITIONS OF THE JOINTS AND MUSCLES

In those affected with hypoplasia of the mesenchyme the fibrous structures supporting the joints are unusually loose, and the range of motion in the joints is greater than is found in the average normal person of a similar age and physical type. This laxity of the ligaments in some families leads to frequent sprains and dislocations. In the first description of the condition Spurway [1] stated that the members of his unfortunate family suffered from bruises and sprains without number. One member of the family suffered a dislocation of the elbow.

Conlon [25] reported a dislocation of the hip associated with a fracture of the femur in a girl, aged 12, who was a member of his family. The injury resulted from a fall of only a few inches, but he laid no stress on the occurrence of a dislocation in this family. Behr [33] in 1913 first emphasized the fact that the joints in these cases are often abnormal. His patient was a small undernourished woman, aged 38, who had had dislocations of the foot, knee, right shoulder and recurrent dislocation of the left shoulder. The family history was not given but the fact that the patient developed otosclerosis at 19 years leads us to include her in the hereditary group. As the roentgenograms of the joints showed no abnormality of the bone, Behr concluded that the joint capsules were at fault and that the condition was a congenital defect due to a disturbance of the internal secretions.

In the Currie family reported by Bronson [5] dislocations were almost as frequent as fractures, and occurred only in those members who had blue sclerotics and brittle bones. This observation of Bronson's to the effect that dislocations are almost as frequent as fractures has not been borne out by other observers, as few instances are recorded in the literature. Freytag [34] reported a case in which the patient had dislocation of the patella at 2 years of age. In one of Singer's [18] patients a dislocation of the clavicle occurred at 5½ years, and one dislocation of the shoulder occurred in a member of the second family reported by van der Hoeve and de Kleijn.[9] From these meager reports one would judge that dislocations are rather rare among these cases.

Sprains are perhaps slightly more common than are dislocations. They were first noted by Spurway,[1] and Cockayne [17] from the large number of sprains which occurred in the family studied by him concluded that the ligaments were abnormally weak and that there was

defective development of all of the mesoblastic tissues. Sprains were frequent in both of the families reported by Bronson,[5] and one of the members of the second family stated that he sprained his ankles frequently and that they caused him more trouble than did his fractures. The sprains occurred only in the members affected with blue sclera and brittle bones. Other than in the few instances mentioned sprains and dislocations have not been noted by other observers nor were they noted in our family. It is probable that the tendency to dislocations and sprains is a prominent feature in only an occasional family.

Hypotonicity of the joints was noted by Cockayne, and he considered the fibrous structures around the joints to be unduly thin and weak. Bronson noted hypotonicity of the joint ligaments in her families, and in Freytag's case the joints of the hand were hypermotile. In our case there was hypermotility of all of the joints except the elbows, in which extension was limited by bony deformities from old fractures (figs. 1, 2 and 3).

The muscle power in our case seemed to be about normal except in the lower extremities in which there was moderate atrophy of disuse. The unusual amount of motion in the joints leads one to suspect that the tone of the muscles is less than normal. However, the deep reflexes are present and it is possible that the fault lies entirely in the fibrous tissues supporting the joints.

11. ROENTGENOGRAPHIC APPEARANCE OF THE BONES

The most complete roentgenographic study of the skeleton in cases of hypoplasia of the mesenchyme is embodied in the short article of Stenvers,[23] who studied the cases of van der Hoeve and de Kleijn. The value of his descriptions is lessened by the omission of all clinical records, and even of the age and sex of the patients. He simply described briefly a number of bones from some members of two families. The left femur presented a marked outward bowing of the shaft and the trochanter was represented by a slight swelling. The femoral head was spherical and the bone structure was coarsened. The epiphyses were swollen and foamy in structure, in contrast to the dense diaphysis. Irregular areas of thickening of the cortex of the femur and fibula marked the site of old fractures. The compacta of the tibia was very thick and showed old fracture lines.

The pelvis was asymmetrical and showed old fracture lines. The spine showed angular scoliosis such as follows a crushing fracture. The skull was remarkable in that there was a definite angulation of the occiput and at the apex of the angle a clear fracture or vessel line was to be seen. The entire vestibular region of the petrous bone was obscured by an unusually thick compact mass which was believed to be an abnormal calcification of the vestibular region.

Several other authors have mentioned and illustrated the roentgenograms of certain bones. Conlon [25] stated that in his case the long bones presented a thin cortex and a broadened medullary canal. On the shaft of the femur were irregular enlargements over which the cortex was very thin. The epiphyses were much broadened and devoid of a cortical outline.

Cockayne [17] noted that in his family the long bones that showed no evidence of fracture exhibited no trace of rickets and were normal except near the ends where they were more transparent than normal. Somewhat similar findings were recorded by Reye [35] whose case showed high grade atrophy affecting only certain bones, and the atrophy was most pronounced near the ends of the diaphysis where the fractures usually occurred. Bronson [5] did not describe the roentgenograms of the bones in any of her cases but some of her illustrations show rarefaction of the bones.

Voorhoeve [10] described a very thin cortex which stood out sharply from the surrounding tissues. The bones contained only a slight proportion of lime salts and showed a rarefaction of trabeculae. In certain fractures little or no endosteal but very strong periosteal callus had been formed. A somewhat similar picture was present in the case reported by Hass.[20] The long bones were very short with a broad marrow cavity and a thin cortex (excentric atrophy). The epiphyses were normal in contour but small and surrounded by a thin shell of compacta. The trabeculae of the epiphyses were decreased in number.

In Singer's [18] case there was a diffuse atrophy of the entire skeleton, with bending of some of the long bones. The only sign of the previous fractures was a sclerosis of the middle third of the left tibia. The skull was unusually long. The base was normal but the vertex was very thin and appeared to be composed of several islands of bone surrounded by dentate suture lines. The inner table was only 1 mm. thick. In the case of Weichmann and Pool [19] the upper third of the shaft of the femur was thin and bowed. The carpal bones were rarefied and the bones of the hand were very thin.

We have roentgenograms of the entire skeleton of our patient. The skull is normal in contour and there is no evidence of old fractures. The bones of the skull and face are thin and less dense than normal. The paranasal sinuses and mastoid cells are well developed. There is no abnormal sclerosis of the petrous portion of the temporal bone. In the vertex the suture lines are rather faint and the region of the lambdoid suture is occupied by a number of unusually large wormian bones which are similar to the bone islets present in Singer's case. The external table is thin over the occiput. The sella is normal. The teeth are normal.

The spine shows no scoliosis or kyphosis. The bodies of the vertebra are definitely smaller than is normal for a person of 12 years. They are of about the normal density and are of the heavy type (broad and short). The laminae and spinous processes are normal and no spina bifida is present. In the lumbar region the transverse processes are small and short (fig. 9).

The ribs are of normal density but unusually slender, especially in the region of the posterior angle. The upper five ribs abruptly sag

Fig. 9.—Pelvis: normal contour, coarseness of bone structure and bilateral coxa valga should be noted.

downward and inward from the posterior angle. The bone structure of the ribs is coarsened.

The clavicles are slender and have a thick dense cortex and a narrow central canal. In each there is evidence of an old fracture of the middle third. At this point the cortex is thickened and there is a break in the line of the bone. The scapulae are normal.

The shafts of the humeri are slender while the epiphyses are of about the normal size. In the shaft the cortex is relatively thickened and the marrow cavity is reduced in diameter. The bone structure is

coarsened, especially in the lower portion of the diaphysis where the large trabeculae are clearly visible. There is no evidence of the old fractures (fig. 10).

In the region of the elbow the epiphyses are all united and the bone is of normal density. The coronoid processes are unusually large.

Fig. 10.—Right elbow: deformity and concentric atrophy of the long bones should be noted; the striation of the thick cortex is faintly visible.

There is a gentle posterior bowing of the shafts of the ulnae, which is more marked on the right side. With the forearm pronated the head of the radius projects one-fourth inch (0.6 cm.) beyond the external condyle. The shafts of the bones of the forearms are slightly less in

diameter than is normal and have a thick cortex and a narrow marrow cavity. In structure the cortex is faintly striated; the striations run parallel with the long axis of the bone. The lower ends of the bones of the forearm and the carpal bones are normal. The metacarpals and phalanges are rather slender and the cortical bone presents the longitudinal striations mentioned above (fig. 11).

Fig. 11.—Right hand: the bones are slender and the structure coarsened.

The pelvis is broad and symmetrical and of the normal female type. There is no evidence of any fractures or of deformity due to softening of the bones. The sacrum is set unusually high as though it had slipped upward about one-fourth inch. The pubic rami are rather

slender. The bones are definitely more radiant than normal and the trabeculae are larger and fewer in number than normal. In the region of the sacro-iliac joints the bone is coarsely granular in appearance (fig. 9).

The two femora are similar in size and contour. The femoral head is rather small (diameter, $1\frac{11}{16}$ inches on the plate), and faces directly upward, the epiphyseal line being approximately horizontal. The neck is rather narrow (diameter, 1 inch), and is in a valgus position (collodiaphyseal angle, right 165 degrees and left 150 degrees). The great trochanter is large and is not yet united. The lesser trochanter is united to the shaft. The diaphysis is slender (diameter, three-fourths inch), and the marrow cavity is narrow (one-quarter inch diameter), occupying only about one third of the width of the bone. The lower end of the femur is approximately normal. There is a slight genu varum (fig. 6). The density of the bone is perhaps slightly less than normal and the bone structure of the cancellous bone is coarser than normal. The patella is small.

The leg bones have been fractured frequently and present different deformities. In the upper third of the left tibia there is a fracture that is not united. The fibula is united. In the region of the fracture there is an anterior bowing of 60 degrees. The shaft of the tibia is rather slender and the cortex is thin, especially on the anterior convex surface. In the region of the fracture the bone ends are unusually dense and the marrow cavity is obliterated by sclerotic bone. The bones are less dense than normal and the cortex is striated (fig. 5).

In the right leg the bones are bowed anteriorly 70 degrees, the deformity being a long curve in the lower half of the leg. The fibula is thin except in the region of the deformity, where it is thickened. The tibia is rather slender but is definitely denser than that of the left leg. The cortex is thickened anteriorly in the upper half and posteriorly on the concave side of the curve in the lower half. In the region of the deformity the bone is sclerotic and the narrow marrow cavity is crossed by frequent trabeculae. The cortex is striated. The epiphyses of the leg bones are decreased in density but normal in other respects (fig. 4).

The bones of the feet are markedly decreased in density and the shafts of the metacarpals and phalanges are very slender. While our patient was under observation we studied roentgenographically the healing of the operated bones and of the incomplete fracture in the tibia.

In the incomplete fracture (fig. 4) the bone united with no visible callus; the ends simply grew together and the fracture line disappeared.

In the fracture caused by the osteoclast there was a small amount of periosteal callus formed on the mesial and lateral aspect of both fragments (fig. 8).

The osteotomy of the tibia seemed to grow together also with a minimum of callus when viewed from the lateral aspect, but on anteroposterior view disclosed fairly extensive periosteal callus on both sides of the fracture. Endosteal callus also seemed to be definitely present. The separated ends of the fibula united by a massive callus (figs. 7 and 8).

In the left tibia where the bone ends were reshaped and screwed together a fairly extensive callus was quickly formed. It extended around the bones and filled the space between them. The fibula in this case threw out an extensive periosteal callus on the inner side of the fracture (fig. 6).

In our patient the bones of the skull and face are thinner than normal. The short bones are about normal though perhaps a little decreased in size, and the long bones have epiphyses that are approximately normal, but the diaphyses all show definite concentric atrophy. The density of the bones is about normal for bones of the same size, except in the lower extremities where the bones are decreased in density. This lack of the normal amount of mineral matter in the leg bones is probably an atrophy of disuse, as our patient had not walked for about three years. An unusually coarse structure of the cancellous bone was noted in our case. There was also an abnormal striation of the cortex of some of the long bones.

It is to be noted that the bones described in the literature fall into two groups: eccentric atrophy with a thin cortex and a wide marrow cavity, and concentric atrophy with a rather thick cortex and a narrow marrow cavity resulting in an unusually slender diaphysis. At present it is not possible to say whether or not either type is characteristic of a given family, or which type is the more common.

12. PATHOLOGY

Other than the descriptions of the sclerae referred to above, the pathology of the tissues in the hereditary hypoplasia of the mesenchyme is not in the literature. From the two operations performed on our patient we obtained specimens of the bone, the skin and scar tissue, the tendon of achilles and striated muscle.

Gross Examination of Bone.—The surface of the tibia is less smooth than normal. The periosteum is adherent but friable and when pulled off small bits remain attached to the bone. The cortex is unusually thick and very hard. The brittleness was evident when in attempting to cut a fragment with a sharp chisel the bone was broken rather than cut. On section the cortical bone appeared to be unusually

porous, being perforated with numerous canals easily visible to the eye. No typical cancellous bone was obtained.

Microscopic Examination.—A small piece of bone was cut in thin cross and longitudinal sections with a jeweler's saw. The sections of the dried bone were then ground on a hone until they were very thin. They were then dried and mounted in balsam. The rest of the tissue was fixed in Zenker's fluid. The bone was decalcified in hydrochloric acid in 95 per cent alcohol solution. Small pieces left in Muller's

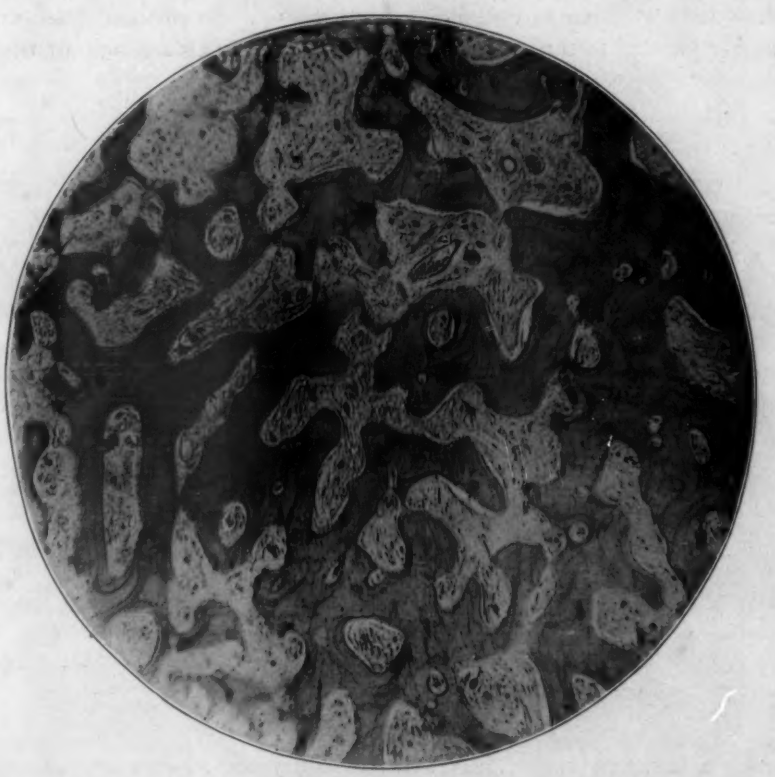


Fig. 12.—Cortex of right tibia (cross section): the numerous wide canals containing a very vascular connective tissue should be noted (32 mm. objective).

fluid were not decalcified after three months. The tissue was embedded in paraffin or celloidin and sections were stained by a variety of methods. All sections examined showed an unusually thick cortex which was penetrated by a great number of wide canals and resembled embryonic bone. In the main these canals ran parallel to the long axis of the bone but by means of large transverse and oblique branches they communicated freely with one another, with the marrow cavity and with the periosteal surface—Volkmann's canals (figs. 12 and 13). The

cross and oblique canals are so numerous that it is often difficult to determine whether a given section is a cross or a long section of the bone. In the dense bone between the larger canals a few typical haversian canals are present. These, too, run irregularly through the bone and in some instances can be seen to communicate with the large canals. In some areas large dense masses of bone are seen in which no canals are present.

The wide canals contain a delicate myxoma-like connective tissue (figs. 14 and 15). This tissue is very vascular and in some of the larger canals twenty or more vessels may be present. The larger vessels run roughly parallel to the axis of the canals but some of the smaller vessels

Fig. 13.—Cortex of right tibia (longitudinal section): a strip of adherent periosteum is present in the upper part of the picture (32 mm. objective).

pursue a tortuous course. Not infrequently the vessels are arranged in bundles of an artery and two or more veins. Each bundle is surrounded by a delicate connective tissue sheath, and several of these may be present in a large canal.

The walls of the arteries are normal in structure but are perhaps a little thinner than are normal arteries of the same size. The veins often appear widely dilated and their walls are extremely thin. In certain instances veins with a diameter of 1.5 mm. have walls that appear to be composed of only a single layer of endothelium which rests on the delicate connective tissue filling the canal. A striking asymmetry is present in the walls of some of the larger veins, one wall consisting of fifteen or more layers of cells and fibers while the opposite wall

consists of only a single layer of endothelium resting in a basement membrane of a few connective tissue cells and fibers.

In addition to the arteries and veins, a number of lymphatic vessels are present in the large canals. They are variable in size and all have thin walls. Some of them are empty, others contain a thin coagulum which stains like fibrin.

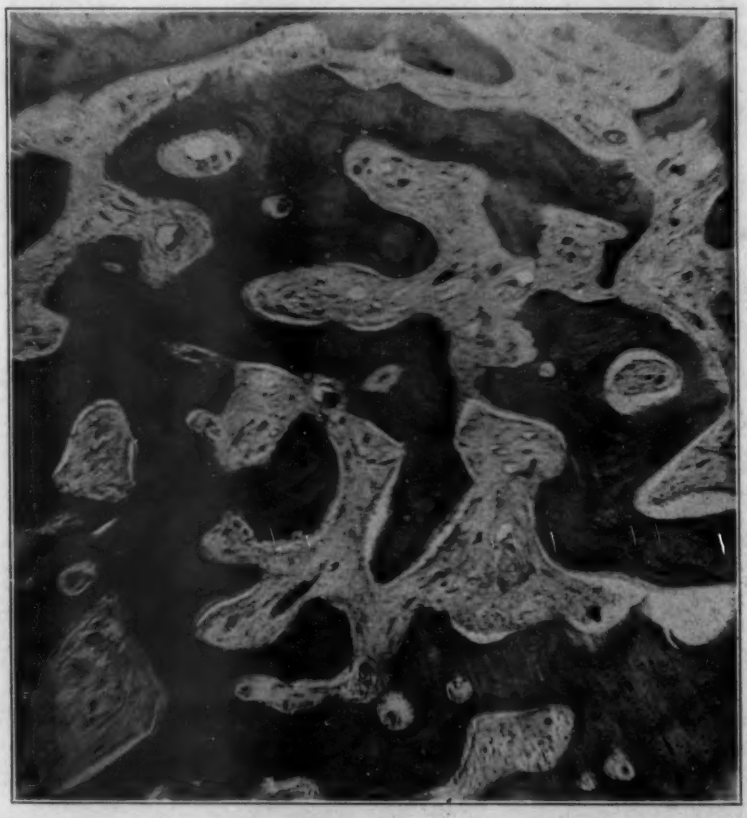


Fig. 14.—Right tibia (cross section): the area occupied by the wide canals is almost equal to that occupied by bone (16 mm. objective).

The groundwork of the connective tissue in the canals is made up of delicate collogenic fibers. They are not wavy and are not arranged in dense bundles as collogenic fibers elsewhere are. They form a loose network in the canal and in some areas are arranged in sheaves or whorls.

In sections stained by Weigert's method for elastic tissue a few dark brown or black fibers can be demonstrated in the loose connective tissue.

These fine elastic fibers tend to run parallel to the long axis of the canal, but may cross or even branch dichotomously.

The loose connective tissue is sparsely populated by cells. The majority of these appear to be young connective tissue cells or fibroblasts. They are spindle or stellate in shape with a large round or

Fig. 15.—Cortex of left tibia (longitudinal section): There are periosteum above, a wide canal in the center filled with delicate connective tissue and four small haversian canals near the surface (8 mm. objective).

oval vesicular nucleus and slightly eosinophilic cytoplasm. A moderate number of mature connective tissue cells with small deeply staining nuclei and thin elongated cell bodies also are present.

In addition to the fixed connective tissue cells a moderate number of round or ovoid wandering cells are present in the loose matrix. A

few of these are small lymphocytes. Others are slightly larger with round or ovoid nuclei and slightly basophilic cytoplasm (primitive cells or plasma cells or larger lymphocytes). The majority of these wandering cells are apparently monocytes with a large kidney shaped nucleus. Occasional osteoblasts and osteoclasts are seen lodged in the connective tissue far from the bony wall of the canal.

Fig. 16.—Cortex of left tibia (cross section of a large canal lined by osteoblasts and containing numerous blood vessels): the irregularities of the bone lamellae should be noted (8 mm. objective).

In a few of the larger canals small collections of fat cells are seen. The fat cells are most often found in those canals which communicate with the marrow cavity. The bone marrow extends a short distance into the canals and is gradually replaced by fat, which is in turn replaced by the myxomatous tissue described above.

In most places the walls of the large canals are lined by one or more layers of osteoblasts (fig. 16). These are usually arranged as a single layer of flattened or cuboidal cells but in some spots the bone is covered by three or four layers of cells and small pockets or recesses in the bone may be completely filled by osteoblasts. They have rather large, deeply staining nuclei and the protoplasm is like ground glass in appearance and stains a light purple in hematoxylin and eosin preparations. They resemble the osteoblasts of normal bone, but are present in greater number than osteoblasts in normal bone. In some areas the layer of osteoblasts is absent and the delicate connective tissue of the large canal is in direct contact with the bony framework. The smaller canals, which we regard as typical haversian canals, are not lined by osteoblasts.

A few osteoclasts are seen in most of the sections. They are large multinuclear cells whose nuclei and cytoplasm resemble the osteoblasts in staining characteristics except that both stain slightly deeper with the hematoxylin. They each contain from three to eight nuclei and as a rule lie on the surface of the bone wall or in Howship's lacunae, but may be free in the connective tissue.

The structure of the matrix of the bone is similar to that of normal bone except that the lamellae are very irregular in their arrangement. They are chiefly ground lamellae which run in every direction and apparently bear little relation to the course of the larger canals (fig. 16). In the thicker areas of bone, the smaller, or haversian, canals are usually surrounded by a series of concentric lamellae. In the case of the large canals the lamellae may run parallel to the wall of the canal, but more often than not they meet the canal at a right or an oblique angle and have no tendency to form concentric layers around the canal.

The organic matrix, like that of normal bone, is made up of alternating sheets of coarse collagenic fibers. Each sheet consists of a single layer of parallel fibers and the fibers in alternating layers tend to be at right angles to one another. In Weigert preparations an occasional dark brown elastic fiber is to be seen coursing through the bone matrix.

In the superficial portion of the cortex Sharpey's fibers are present. In sections stained with Mallory's phosphotungstic acid hematoxylin they are seen as coarse reddish brown collagenic fibers which run from the periosteum to the bone. They stain as does the bone matrix but can be traced for some distance into the bone, running through the layers of lamellae.

The bone cells are about as numerous as in normal cortical bone and lie in lacunae that have their long axes parallel to the enveloping lamellae. In the interlamellar areas where the groundwork has no definite structure the lacunae are shorter and thicker and may be roughly spherical in shape. In thinly ground sections of dried bone,

and in sections of decalcified bone stained by Schmorl's thionin method, the intercellular canaliculi are visible (fig. 17). These minute canals are thickly set around the periphery of the lacunae, running out in all directions, pursuing a wavy course, and uniting with the canaliculi from

Fig. 17.—Bone lacunae and canaliculi stained by Schmorl's thionin method: in the upper picture the canaliculi pass from one lacuna to another; in the lower picture the canaliculi are mostly seen in cross section (2 mm. oil immersion).

neighboring lacunae. In many instances canaliculi from two neighboring lacunae not only are continuous but send off branches that unite with similar branches from canaliculi on either side, thus forming a most intimate anastomosis. In properly stained sections the bone cells can

be seen to send protoplasmic processes into the canaliculi, and it is probable that in the living state the bone cells form a true syncitium; though I have not been able to demonstrate direct protoplasmic continuity between the cells in sections. In areas in which the lacunae are arranged in different planes, the canaliculi can often be traced across a row of lacunae in a different plane to unite with the canaliculi from the next row that lie in the same plane. The lacunae that lie close to the large canals communicate with them by means of numerous canaliculi which open into the canals. This is true of both the haversian and the larger (Volkmann's) canals.

A section from the site of the nonunion in the right tibia presents a border of dense sclerotic bone 5 mm. in thickness. This sclerotic bone is not lamellated in structure and contains no canals or nutrient vessels. It is sparsely populated by cells. In some areas near its free border the cells are arranged in rows or nests as is typical of cartilage though here the matrix is definitely calcified.

Between the eburnated border zone and the rest of the shaft there is a zone of very atrophic bone where bone absorption and formation is in progress. The bone absorption is being carried on by osteoclasts which appear to be eroding some of the lamellae. The new bone is for the most part being formed by osteoclasts in the typical manner. In other areas the bone is being laid down in membrane or by calcification of connective tissue. A small calcified area is surrounded by a network of radiating fibers which gradually merge with the surrounding tissue of the large canals. From the center outward bone cells, osteoblasts and typical fibroblasts are met with. Apparently all transitions exist between these three types of cells.

At the operation the periosteum was found to be firmly adherent to the bone, but it was unusually friable and bits of it could be pulled off with tissue forceps. It was pinker and more delicate than is the fibrous periosteum of normal bone. Microscopically, it resembled normal periosteum and was composed of an outer fibrous and an inner reticular layer (fig. 18). The outer layer was made up of coarse, wavy collagenic fibers, most of which ran parallel to the long axis of the bone. It contained a moderate number of mature connective tissue cells. The inner layer was made up of delicate collagenic and elastic fibers which formed a loose reticulum. Here the connective tissue cells were more numerous and of a younger type than the lamellar cells of the outer layer. A few wandering cells also were present. Next to the bone cortex was a layer of osteoblasts. They resembled those of normal bone in size, number and arrangement. A number of coarse collogenic fibers from the outer layer crossed the reticular layer and extended into the bone (fibers of Sharpey). At the places where the large canals (Volkmann's) opened on the cortex, the reticular layer of

the cortex was continuous with the reticular tissue filling the canals, while the fibrous layer of the periosteum spanned the openings without dipping into the canals. The blood and lymph vessels lay in the reticular layer and were normal in size and number.

The tendon of achilles was unusually small, the diameter being about one-fourth inch. In the fresh state it was light pink and trans-

Fig. 18.—Cortex of left tibia (longitudinal section): The periosteum is shown above; the irregularity of the bone lamellae should be noted (8 mm. objective).

lucent in appearance. The dense white fibers of normal tendon were not present. On microscopic examination, both in cross and longitudinal sections the tendon appeared to be approximately normal. The fibers were normal in size and appearance, and were grouped in irregular bundles as are those of normal tendon. They reacted normally to the various connective tissue stains. There was perhaps a slight increase in the vascularity of the tendon, and the connective tissue cells were more numerous than usual but normal in size and arrangement.

The skin and subcutaneous tissue were studied by a wide variety of technics. The stratum corneum was rather thick but otherwise normal. The rete mucosum was normal. In the cutis vera the elastic fibers seemed to be somewhat larger and more numerous than usual. This was especially well shown in sections stained by Verhoeff's method for elastic tissue and then counterstained with acid fuchsin to render the collagenic fibers prominent. In such a section compared with a section of normal skin treated in a similar manner there seemed to be an increase in the elastic fibers and a decrease in the collagenic fibers. The hair follicles, sweat and sebaceous glands and blood vessels were normal. Nothing abnormal was noted in the subcutaneous tissue.

The scar tissue was unusually friable on gross examination but microscopically consisted of dense collagenic tissue and was sparsely supplied with minute blood vessels. It contained no elastic fibers.

The striated muscle showed no abnormalities on histologic examination.

13. OTHER ABNORMALITIES

As a rule the general medical examination in these cases is negative. Bronson [5] raised the question of the presence of arteriosclerosis in these people on the basis that if calcium was deposited in the ear it might also be found elsewhere—in the arteries. Her families were free from arteriosclerosis and it has not been found by others. Hass [20] emphasized the frequency of heart failure in his family. Of twenty-four members in three generations seven had died of heart failure and the mother and an uncle of his patient both had valvular heart disease.

Marconi [37] noted defective development of the circulatory apparatus in a young soldier with blue sclera and a history of several fractures. In our case the heart and blood vessels were normal to physical examination, but it was noted at operation that the vessels were very friable. A hemostat on the end of a vessel could be pulled off with little force. The history in our case that she bruised easily also suggests the presence of weakness of the vessel walls.

Abnormal calcification was noted by Weichmann and Pool [19] in the lungs of their patient. The roentgenogram of the chest showed pea sized angular shadows scattered over the whole lung area. They were able to obtain no history of tuberculosis in this patient and considered the shadows to be calcified masses—calcium metastases in the sense of Virchow,[38] who noted that in cases with severe bone atrophy there was a tendency for calcium to be laid down in abnormal locations in the

37. Marconi, A.: Gazz. d. osp. **39**:367 (May 9) 1918; abstr., J. A. M. A. **71**: 319 (July 27) 1918.

38. Virchow, quoted from Wells, H. G.: Metastatic Calcification, Arch. Int. Med. **15**:574 (April) 1916.

body. These calcium metastases have not been noted by other observers, unless we consider the otosclerosis as being such.

A macular atrophy of the skin was present in the case of Blegvad and Haxthausen.[39] The patient was covered with grayish purple spots varying in size from minute spots up to areas 2 cm. in diameter. The base was smooth, sunken below the level of the surrounding skin, and the underlying veins were clearly visible. Microscopically there was an atrophy of the corium. In our case the skin was freckled and rather dry but otherwise normal.

Dentition is, as a rule, normal. In one of Voorhoeves' cases, the jaws were small and the lateral incisors were pointed inward. In the nonhereditary case of Vander Veer and Dickinson[40] the teeth were translucent and obviously lacked mineral salts, and the gums were spongy and bled easily. In Stobie's[24] family some of the members showed deficiencies in the enamel of the teeth and gave a history of the teeth breaking away on biting bread. Crocco[41] noted late development of the teeth. In our case the teeth were normal.

Hemophilia was present in ten members of the large family studied by Voorhoeve. It has not been present in other families and is not yet proved to be a part of the syndrome.

The neurologic examination is as a rule negative and the intelligence is normal. The only exception in the literature is the case of brittle bones and blue sclera in a mongolian idiot reported by Bolten.[42] (I am not sure that this case was of the hereditary type.)

Infant Mortality.—Bronson noted that in her family there was an abnormally high infant mortality rate among the affected members as compared with the normal members. In the family of Hass there were ten deaths in infancy or early life among the twenty-four persons. Tuberculosis was of frequent occurrence in the family of Voorhoeve.

Congenital Anomalies.—In one of the families of van der Hoeve and de Kleijn there were seven cases of syndactylism. Voorhoeve noted cleft palate three times, an adduction of the little fingers once, and rachischisis twice in his family. One of Blencke's cases had congenital torticollis.

---

39. Blegvad, O., and Haxthausen, H.: Blue Sclerotics and Brittle Bones, with Macular Atrophy of the Skin and Zonular Cataract, Brit. M. J. **2**:1071 (Dec. 24) 1921.

40. Vander Veer, E. A., and Dickinson, A. M.: Fragilitas Ossium, Ann. Surg. **74**:629 (Nov.) 1921.

41. Crocco: Blau sklera, Comm. d. Hosp. Ophth. Buenos Aires **2**:38, 1920, quoted from Blenke.

42. Bolten, G. C.: Het Voorkomen von blauwe Sclerae, Nederl. Tijdschr. v. Geneesk. **1**:560 (Feb. 23) 1918.

Laboratory Findings.—No abnormalties have been noted in the urine in these cases and none was present in our case. A number of authors have commented on the slight lymphocytosis present. In our case 34 per cent of the white blood cells were lymphocytes. We do not consider this unusual in a child. Thinking that perhaps there might be some abnormalities in the white blood cells, the blood was examined by the supravital technic several times. The living cells exhibited motility, contained the usual amount of mitochondria and reacted to neutral red as do the normal blood cells. The calcium and phosphorus content and the hydrogen ion concentration of the blood in our case were normal, the blood clotting time was normal and the basal metabolism was normal.

14. DIAGNOSIS, PROGNOSIS AND TREATMENT

The diagnosis is made by the presence of an abnormal bluish tint of the sclera which was also present in one or both parents. The presence or absence of fractures or other stigmas is not necessary for the diagnosis.

The prognosis is that acute fractures will unite quickly. After the patient reaches the age of puberty it is probable that the fractures will cease to occur, though there are several cases on record in which fractures from minor forces have occurred in adult life. It is certain that if an affected person has children, approximately half the children will be afflicted with the condition.

Treatment.—The patient should be advised to lead a normal life but to refrain as much as possible from subjecting the bones to trauma. Drugs, chemotherapy, vitamins, diet, light rays and endocrine preparations have been tried. No form of treatment is known to have any effect on the condition. Acute fractures should be treated just as though the patient were normal. The treatment should be prompt and the period of immobilization can be shortened, as the bones tend to unite quickly. Deformities, if present, should be corrected. These patients stand operations well and there is no cause to fear nonunion after osteotomies. As a measure of prevention these unfortunate persons should be told that if they marry and have children at least half the children may be expected to be afflicted with hypoplasia of the mesenchyme.

15. COMMENT

The term "hereditary hypoplasia of the mesenchyme" is used to describe the condition usually called brittle bones and blue sclera. This is because it has been shown that in these cases many of the mesenchymal tissues may be underdeveloped.

This type of fragilitas ossium is hereditary and in addition to the brittleness of the bones is characterized by blue sclera, small stature,

hypermobility of the joints and a weakness of the fibrous structures throughout the body. The cases that reach adult life tend to develop progressive deafness.

The hereditary factor is a dominant one. The condition is inherited directly from an affected parent. Of children one of whose parents is affected with blue sclera, 62 per cent are born with blue sclera and 42 per cent suffer multiple fractures. There is no skipping of generations and the children of affected parents who are themselves not affected do not transmit the condition to their offspring.

The blue appearance of the sclera is not due to a deposit of pigment but is due to an abnormal translucency of the fibrous tissue which permits a shining through of the deeper tissues. From observations in the fascia and tendons in our case it is probable that the sclera is thinner than normal and is of an abnormal quality.

The fractures in these cases are not spontaneous but are due to definite causes. In most instances, however, the violence causing the fracture is less than would be necessary to break a normal bone. The deformities are due to malunion of old fractures and not to softening of the bone. Roentgenograms of the skeleton in our case showed a general decrease in the size of the bones, a thinning of the skull, and a concentric atrophy of the long bones.

There was cortical striation of compact bone and coarseness of structure of spongy bone. The bones that had not been subject to disuse showed little rarefaction. There are cases in the literature in which the bones are reported as being rarefied and exhibiting eccentric atrophy. Whether or not the two types occur in the same family is not known. There have been no adequate roentgenographic reports on several members of a family. Such studies are needed to clear up this phase of the subject.

Examination of the bone removed at operation from our patient showed it to be unusually hard and brittle. The structure was similar to that of normal bone except that the lamellae were irregular in arrangement and the amount of compact bone was decreased by the presence of numerous large canals. The cortex of the tibia was honeycombed with large canals which contained a very vascular connective tissue.

The presence of these canals explains the cortical striations seen in the roentgenograms. They also partly explain the ease with which the bones are fractured. The irregularity of the lamellae probably renders the bone less strong than normal. A third factor is the probability that there is some abnormality in the quality of the fibrous matrix of the bone. This is suggested by the observation that the tendon of achilles was pink and translucent in appearance and much reduced in diameter: on microscopic examination, however, the fibrous structure of the tendon was normal in appearance. The nature of the abnormality in

the quality of the fibrous tissue is not known. It is probable that it involves all the collagenic tissue in these patients and explains the friability of the blood vessels, fascia, periosteum and subcutaneous tissues noted in our case.

The rapid healing of the fractures in these cases is explained by the presence of large numbers of osteoblasts in the wide canals of the cortical bone.

The blood of our patient was examined several times and the hydrogen ion concentration and calcium and phosphorus content were always within normal limits. The p_H tended to the alkaline side of the normal range and the calcium and phosphorus tended to be a little high.

From our studies hypoplasia of the mesenchyme seems to be an anomaly of development rather than a derangement of metabolism. The hypoplasia is apparently limited to those tissues derived from the mesenchyme. We have found no evidence of any endocrine disturbance in our patient. It is certain that the condition exists in varying degrees in different individuals who are affected with the hereditary type of blue sclera. It is probable that those who have not had fractures have abnormalities in the structure of the bones similar to those present in our case. That they have not had fractures is due either to the condition being less in degree or to the fact that the bones have been subjected to less trauma.

From what has been said above it is probable that hereditary hypoplasia of the mesenchyme is in no way related to any of the acquired forms of bone fragility. We have then to consider its possible relation to osteogenesis imperfecta and to idiopathic osteopsathyrosis. In spite of the opinions of numerous German authors that these two conditions have the same pathologic basis, it seems better to consider them as separate conditions because they certainly present different clinical pictures.

In regard to osteogenesis imperfecta, it is to be noted that this condition is not known to be hereditary. The typical patient is born of apparently normal parents and presents numerous fractures at birth or in infancy. Most of the patients die in infancy and so cannot transmit the condition. Furthermore, no case of osteogenesis imperfecta has been recorded in any of the families afflicted with hereditary hypoplasia of the mesenchyme.

In idiopathic osteopsathyrosis the fractures occur in childhood and are not as a rule numerous. It is known that some of these patients have blue sclera, and it is probable that they also present other evidence of hypoplasia of the mesenchyme, though this has not been noted in any of the cases reported. The few reports on the bone in this condition resemble the pathologic findings in our case. In brief, our case resembles closely some of the reported cases of idiopathic osteopsathyrosis. The

only known difference is that in our case the condition is a dominant hereditary character. To settle the question of the identity of the two conditions we need a patient with idiopathic osteopsathyrosis with blue sclera and born of normal parents who has transmitted the condition to some of his or her children.

On the other hand, there are cases of nonhereditary idiopathic osteopsathyrosis with sclera of normal color.[43] The question as to whether or not these form a separate group cannot be decided at this time. It is certain, however, that they do not fit into the group which we term hereditary hypoplasia of the mesenchyme.

A fourth and rare type of idiopathic bone fragility is that known as marble bones, or Albers-Schonberg disease. It is probably not hereditary.[44] This is not usually classed as a type of fragilitas ossium but the hardness and brittleness of the bones noted in our case are at least suggestive that the two conditions have some features in common.

From what has been said in the foregoing it is possible to classify idiopathic bone fragility as follows:

1. Hereditary Form: Hereditary hypoplasia of the mesenchyme.

2. Nonhereditary Forms: (*a*) Osteogenesis imperfecta; (*b*) osteopsathyrosis with white sclera; (*c*) osteopsathyrosis with blue sclera.

3. Probably Not Hereditary: Osteosclerosis fragilis generalisata, or marble bones.

16. SUMMARY

From an analysis of the literature it is shown that blue sclera is the only feature of hereditary hypoplasia of the mesenchyme which is present in every case and which is transmitted as a dominant hereditary character.

The other abnormalities are short stature, brittle bones, hypermobility of joints and deafness.

Our observations lead us to believe that idiopathic fragility of bones is due to an abnormality in development rather than to a metabolic disturbance.

---

43. Glover, D. M.: Osteopsathyrosis, Arch. Surg. **5**:464 (Nov.) 1922.

44. Davis, G. G.: Osteosclerosis Fragilis Generalisata, Arch. Surg. **5**:449 (Nov.) 1922.

THE RELATIONSHIP BETWEEN VERTEBRAL EPIPHYSITIS AND SPINAL DEFORMITY *

JOSEPH BUCHMAN, M.D.

Assistant Surgeon in Outpatient Department, Hospital for the Ruptured and Crippled, New York; Associate Attending Orthopedic Surgeon and Chief of Clinic, United Israel Zion Hospital, Brooklyn

BROOKLYN

The presentation that I [1] made a year ago led to the conclusion that vertebral epiphysitis is a disease entity, and that it may be a cause of spinal deformity. That the former is a reasonable conclusion is becomis more and more evident from a perusal of the French,[2] German [3] and Italian [4] literature in which there has recently appeared a pertinent series of independent observations leading to the same belief. A number of authors have doubted that vertebral epiphysitis is a cause of spinal deformity. It is my purpose here to stress this phase of the subject and to bring more data to bear on this question.

Scheuermann [5] in his original article on kyphosis dorsalis juvenilis raises the issue as to whether vertebral epiphysitis is a cause or a result of spinal deformity. He answers it in the affirmative without presenting definite evidence in proof thereof. Haglund [6] in discussing Scheuermann's work asks the same question, but makes no attempt to answer it. More recently, my friend and teacher Dr. Kleinberg [7] states:

> It is possible that the described changes in the vertebrae represent a disease process or entity, and as such could be the cause of many cases of idiopathic scoliosis. On the other hand, the alterations in the vertebral morphology may be

---

* Read before the Orthopedic Section of the New York Academy of Medicine, Jan. 15, 1926.

1. Buchman, Joseph: Vertebral Epiphysitis; A Cause of Spinal Deformity, J. Bone & Joint Surg. **7**:814 (Oct.) 1925.

2. Mathieu, Paul; Massart, and Ducroquet, R.: La Cyphose douloureuse et L'épiphysite Vertébrale de Croissance, Bull. et mém. Soc. nat. de chir. **51**:220 (Feb. 28) 1925.

3. Mau, C.: Die Kyphosis dorsalis adolescentium im Rahmen der Epiphysenlinienerkankungen des Wachtumsalters, Ztschr. f. orthop. Chir. **46**:145, 1924; Die dorsale Kyphose der Adoleszenten, München. med. Wchnschr. **72**:211 (Feb. 6) 1925; Die dorsale Kyphose der Adoleszenten, Ztschr. f. Chir., 1924, p. 359. Hahn, Otto: Kyphosis Osteochondropathica, Klin. Wschnschr. **1**, May 27, 1922.

4. Valtancoli, G.: L'osteochondrite Deformante Giovanile Vertebrale, Riforma med. **41**:823 (Aug. 31) 1925.

5. Scheuermann, H.: Kyphosis Dorsalis Juvenilis, Ztschr. f. orthop. Chir. **41**, 1921.

6. Haglund, Patrick: Prinzipien der Orthopädie, 1923.

7. Kleinberg, Samuel: Scoliosis, 1926.

part of the deformity that is secondary to or the result of scoliosis. Further study is certainly necessary to enable us to estimate the value of this work, and to decide whether disease of the vertebral epiphyses is a factor in the etiology of scoliosis, and if so, to what extent.

Assuming for a moment that the epiphyseal pathology is the result of deformity of the spine, this condition should at least be present in some of the cases of spinal deformity regardless of its etiology. This is not so, for in both mild and severe deformities following poliomyelitis, Pott's disease, rickets and congenital disturbances, in the same age period, epiphyseal derangements are not found. I and others have found these pathologic changes only in the so-called idiopathic forms.

Again, if it is true that the epiphyseal pathologic condition is the result of deformity, there should be a definite relationship between the epiphyseal changes and the deformity. One should expect that the greater the deformity the greater would be the epiphyseal change, and that the maximum degree of deformity should coincide with the greatest amount of epiphyseal change. Roentgenographic observations fail to sustain this concept. The active stage of epiphyseal changes is commonly seen in the mild deformities and rarely in the severe curves. By the time the severe deformity has developed the acute stage of epiphyseal changes has subsided and nothing but the after effects remain. The wedge vertebra is the end-result of the disease process just as it is in rickets or indirectly in poliomyelitis.

Delahaye [8] originally reported three cases of vertebral epiphysitis without gross spinal deformity. In a later article,[9] he reviewed twenty-five cases of vertebral epiphysitis without spinal deformity. I have seen a number of similar cases, two of which I will present in detail. Patients with mild round shoulders and definite evidence of epiphyseal changes are common in our experience at the Hospital for the Ruptured and Crippled.

All organic deviations of the spine develop in accordance with Delpèche's Law. Excessive pressure causes an arrest or diminution of the activity of the epiphyseal cartilages. Conversely, diminished pressure causes hyperactivity. Therefore, any static disturbance causing unequal pressure on the vertebral epiphyses will cause unequal growth. Just as poliomyelitis, Pott's disease, torticollis and congenital deformities are causes of static disturbances, so, the derangements of the epiphyses as

8. Delahaye, André: Étude sur quelques diagnostiques de mal de Pott en particulier sur l'épiphysite vertébrale de croissance, Travail de l'Hôpital Maritime de Berck, Paris, 1924.

9. Sorrell, Etienne; and Lalahaye, André: Des Épiphysitis de Croissance et en particuier de l'Épiphysite Vertébrale Douloureuse des Adolescents, Presse méd.. Sept. 10, 1924, p. 737.

comprehended under the term of vertebral epiphysitis are causes of static disturbance.

Finally, as further evidence that vertebral epiphysitis is a cause of spinal deformity, I wish to present two previously reported cases with additional data.

Fig. 1 (case 1).—Lateral view, April 20, 1924, showing normal dorsal and lumbar curves, mottling and haziness of upper dorsal intervertebral spaces, indistinct and irregularly thickened upper and lower outlines of dorsal vertebrae and thickened posterior epiphyses; comparison should be made with figure 2.

REPORT OF CASES

Case 1.—E. B., a girl, aged 13 years and 7 months, was admitted to the Hospital for the Ruptured and Crippled in the service of Dr. Royal Whitman because of scar contractions of several of her fingers subsequent to an injury. Her

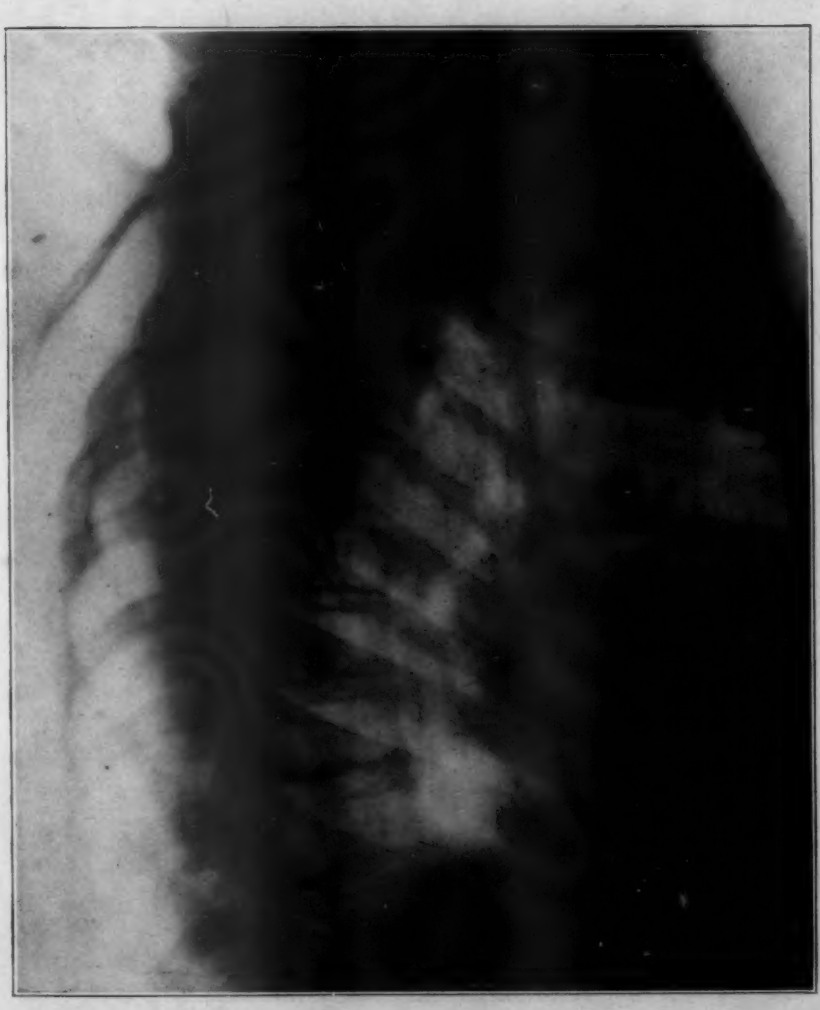


Fig. 2 (case 1).—Oblique lateral view of dorsal region, Feb. 28, 1925, showing mottling of intervertebral spaces and irregularly thickened, motheaten, hazy appearance of superior and inferior outlines of vertebral bodies and superior and inferior epiphyses, i. e., an increase in the roentgenologic pathologic condition.

history was irrelevant save that she had had "growing pains" in the knees and elbows on excessive exertion. Clinically, her back was symmetrical and her spine was negative in all respects.

She was thought a fit subject for our study of normal spines, and consequently was roentgenographed, April 30, 1924. Much to our surprise and temporary confusion the roentgenograms showed in the anteroposterior views that beginning

Fig. 3 (case 1).—Lateral view, Jan. 5, 1926, showing an increase in dorsal and lumbar curves and an increased wedging of dorsal vertebrae.

with the fifth and down to and including the twelfth dorsal vertebrae, the superior and inferior borders of the vertebral bodies were not as distinct as elsewhere, and the intervertebral spaces were diminished, fogged and mottled. The lateral views showed no abnormality in the anteroposterior curves. The twelfth dorsal vertebra was somewhat wedge shaped. On the superior border of the eleventh dorsal vertebra, there was a faint irregular linear thickening which was interrupted

anteriorly. The same was present on the inferior border of the tenth dorsal vertebra, only more distinct. In the ninth intervertebral space, the superior and inferior posterior thickenings were marked and they extended anteriorly as broken lines. The same findings were present in the eighth dorsal intervertebral space. In the seventh, sixth, fifth and fourth dorsal intervertebral spaces the epiphyseal plates were very much thickened, their outlines were indistinct, they were fragmented and the interspaces were mottled and hazy. The superior and inferior borders of all these vertebral bodies were indistinct and irregular (fig. 1).

Feb. 28, 1925, the patient and her mother volunteered the information that they had noticed a tendency to round shoulders. Clinically there was a mild degree of round shoulders which was not present at the first examination. There was definite tenderness over the sacrococcygeal junction and both iliac crests. Roentgenograms

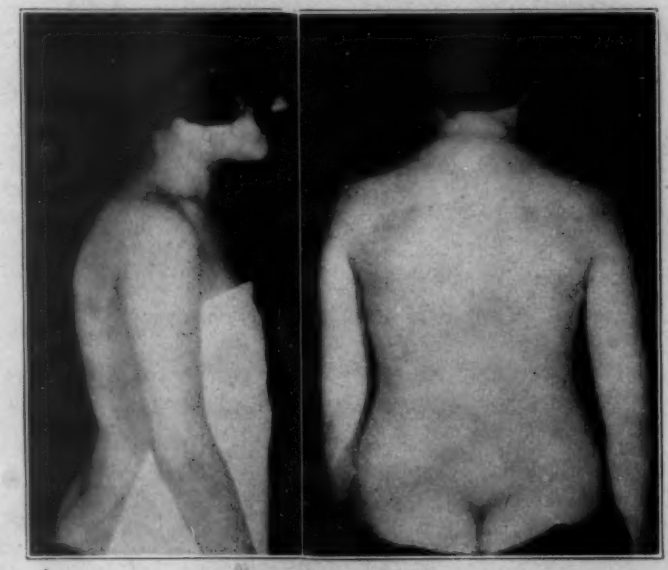


Fig. 4 (case 1).—Appearance of patient, Jan. 5, 1926, showing a moderate grade of round shoulders, which was absent when the patient came under observation.

taken at this time showed an advance in the pathologic condition described and an increase in the normal dorsal curve (fig. 2).

When seen, October 10, the patient had no complaint referable to the spine. Clinically the back was negative save for an increase in the kyphos in the lower dorsal region. Roentgen-ray examination substantiated the increase in curvature. The epiphyseal pathologic condition had changed but slightly since the last examination.

The patient was last seen, Jan. 5, 1926, when no further changes were noted (figs. 3 and 4).

Case 2.—A. D., a boy, aged 15 years, was admitted to the Hospital for the Ruptured and Crippled in the service of Dr. Royal Whitman for treatment for rigid flatfoot. He had recently arrived from Austria where he had undergone a great deal of starvation and privation. He was underweight, tall for his age and somewhat anemic. There was no history referable to his spine and clinically his back was negative.

He was roentgenographed, May 20, 1924, for our normal series of spines. The anteroposterior view showed that beginning with the seventh and down to the twelfth dorsal vertebra, there was a mottled haziness in the intervertebral spaces which were irregular in size. The upper and lower vertebral outlines were indistinct and appeared motheaten. In the intervertebral spaces there were definite darker and lighter areas very much akin to the appearance in Legg's disease. The

Fig. 5 (case 2).—Lateral view, May 20, 1924, showing normal dorsal and lumbar curves, enlarged, frayed and irregular epiphyses in the dorsal region with mottling and haziness of the intervertebral spaces.

lateral view showed normal anteroposterior curves. From the seventh dorsal down to the inferior border of the eleventh dorsal vertebra the anterior inferior and superior, and the posterior inferior and superior epiphyseal plaques were much enlarged, so that there were distinct concavities just behind the anterior and just in front of the posterior plaques, while the intervening areas were convex. All the

outlines were poorly demarcated and within the spaces there were darker and lighter areas. In addition, the vertebral bodies appeared more porous than in the lumbar region, which were apparently negative (fig. 5).

When the patient was seen, March 7, 1925, he complained of occasional fleeting pains in the cervical portion of the spine. He also noted that he had grown considerably during the interval. Examination showed that his posture was poor.

Fig. 6 (case 2).—Lateral view of dorsal region, Oct. 10, 1925, showing an increase in dorsal curve, wedging of vertebral bodies, irregularity, motheaten and indistinct appearance of epiphyses and superior and inferior vertebral outlines.

There was a definite round shoulders hollow back present. Roentgen-ray examination showed an increase in the dorsal kyphosis and the lumbar lordosis. The eighth and ninth dorsal vertebrae were wedged. The vertebral outlines were now sharper, denser and less wavy. The epiphyseal plaques were less thickened, less frayed and less motheaten. The intervertebral spaces showed considerable striation and mottling.

Examination, October 10, showed a further increase in growth and a more marked hollow round back. Roentgenograms showed an increase in the deformity. The middorsal region showed more wedging of the bodies and some increase in the pathologic change shown in the roentgenogram. The upper dorsal region was somewhat improved (fig. 6).

Fig. 7 (case 2).—Lateral view, Jan. 13, 1926, showing further increase in dorsal and lumbar curves; comparison should be made with figure 5.

Jan. 13, 1926, the patient had no complaints. The hollow round back was more marked (fig. 8). The roentgenograms showed an increased kyphosis with an increase in the wedging at the apex of the dorsal curve. The epiphyses could not be distinguished as such (fig. 7).

In reviewing these two cases it is evident (1) that when first observed they presented negative anamneses, negative clinical appearances and a

definite roentgenologic pathologic condition without gross deformities of the spine; (2) that while under observation some clinical evidences of epiphyseal derangements appeared, namely, occasional pain, tenderness and rapid growth in the second case, and (3) that deformity finally developed.

CONCLUSIONS

1. Vertebral epiphysitis is not found in deformities of the spine of known origin, such as poliomyelitis, Pott's disease, rickets, torticollis, congenital deviations and inequality of the lower limbs.

2. The active or acute stage of vertebral epiphysitis is more commonly seen in the milder deformities and less commonly in the severe

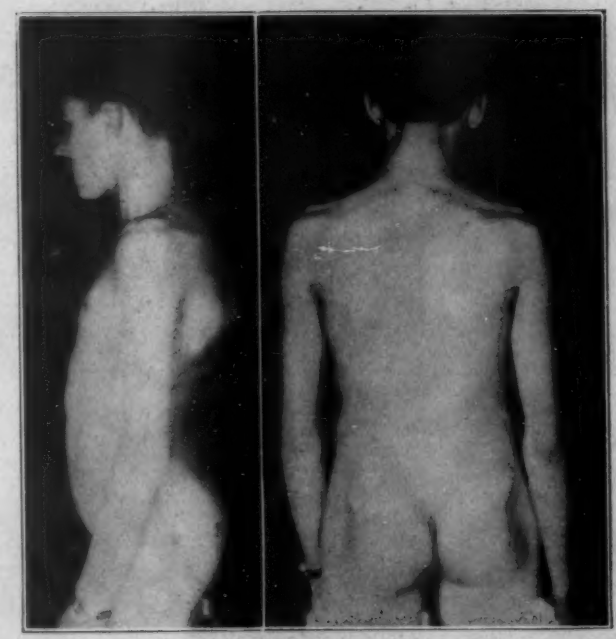


Fig. 8 (case 2).—Appearance of patient, Jan. 13, 1926, showing a marked hollow round back; when the patient came under observation this condition was not present.

deformities. All that usually remains in the severe deformities are the end-results.

3. Vertebral epiphysitis causes a derangement in the epiphyses which starts a cycle of events in accordance with Delpèche's Law and the pathogenesis of the resultant spinal deformities is the same as in rickets, poliomyelitis and Pott's disease.

4. In the two cases with negative clinical and definite roentgenologic symptoms presented, the patients subsequently developed deformities.

5. From the foregoing observations it is my belief that vertebral epiphysitis is a competent cause of spinal deformity.

EXPERIMENTAL ACUTE GASTRIC FISTULA

WALTMAN WALTERS, M.D.
Division of Surgery, Mayo Clinic
AND
JESSE L. BOLLMAN, M.D.
Division of Experimental Surgery and Pathology, the Mayo Foundation
ROCHESTER, MINN.

Changes that occur in the blood in experimental acute gastric fistula are a rise in the carbon dioxide combining power of the plasma, a decrease in chlorides, and an increase in urea. These changes are similar in some respects to those in acute duodenal fistula [1] and to those other observers [2] have found in high intestinal stasis. In experimental acute gastric fistula there is a greater increase in blood alkalinity, as denoted by the carbon dioxide combining power of the blood, due to the loss of acid from the body through the gastric fistula. The decrease in the chloride content of the blood is quite comparable to that in duodenal fistula and in high intestinal stasis. Studies of the fistulous fluid revealed a loss of chlorides sufficient to account for the decreased chloride content of the blood. Because of the pronounced decrease in blood chlorides and the beneficial results obtained by the use of chloride in high intestinal stasis and also in duodenal fistula, we have studied the effect of intravenous injections of chloride solutions in comparison with other control solutions in gastric fistula. Of the various solutions, isotonic sodium chloride solution compensated best for the chemical changes in the blood accompanying acute gastric fistula and assisted most in prolonging life. The amount of nitrogen lost in the urine and in the fistulous fluid remained at approximately the normal level, although there was definite evidence of the retention of nitrogen in the blood.

---

1. Walters, Waltman; Kilgore, A. M., and Bollman, J. L.: Changes in the Blood Resulting from Duodenal Fistula: A Clinical and Experimental Study, J. A. M. A. **86**:186-189 (Jan. 16) 1926.

2. Brown, G. E.; Eusterman, G. B.; Hartman, H. R., and Rowntree, L. G.: Toxic Nephritis in Pyloric and Duodenal Obstruction: Renal Insufficiency Complicating Gastric Tetany, Arch. Int. Med. **32**:425-455 (Sept.) 1923. Haden, R. L., and Orr, T. G.: Chemical Changes in the Blood of the Dog After Pyloric Obstruction, J. Exper. Med. **37**:377-381 (March) 1923; Chemical Changes in the Blood of the Dog After Obstruction of the Esophagus and of the Cardiac End of the Stomach, J. Exper. Med. **38**:477-485 (Oct.) 1923. McVicar, C. S.: A Discussion of the Clinical and Laboratory Findings in Certain Cases of Obstruction in the Upper Gastro-Intestinal Tract: The Rôle of Blood Chemistry in Diagnosis, Prognosis and Treatment of This Condition, Am. J. M. Sc. **169**:224-235 (Feb.) 1925.

Just before death a decrease in the excretion of nitrogen occurred accompanying anuria.

The work of Haden and Orr [3] in experimental high intestinal obstruction showed that the nearer the obstruction to the pylorus the greater the toxemia, which might be explained on the hypothesis that the loss of chlorides in such cases was due to their excretion into the lumen of the stomach and the intestine and loss from the body in that manner, whereas in experimental fistula the chlorides were lost from the body through the fistula. Again, in experimental acute gastric fistula as in acute duodenal fistula, a part is played by interruption in the continuity of the gastro-intestinal tract by the gastric fistula. Studies are now being carried out in an attempt to evaluate the effect of discontinuity of the gastro-intestinal tract.

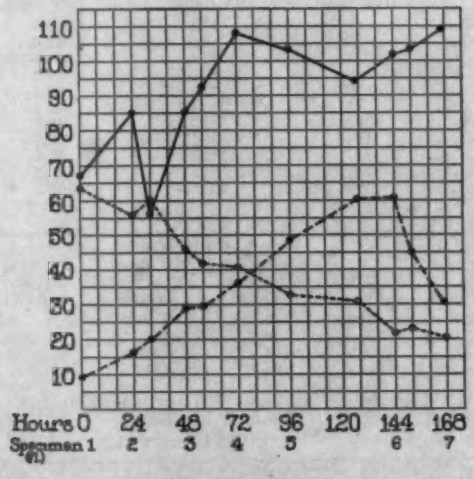


Chart 1.—Chemical changes in the blood in dog with gastric fistula following administration of water through duodenal tube: solid dot solid line, carbon dioxide; solid dot broken line, urea; open dot broken line, chlorides.

METHODS

Gastric fistulas were made on dogs under ether anesthesia, the stomach being isolated and divided at the pylorus. The duodenal stump was turned in as a blind end and the pyloric end of the stomach incorporated in the closure of the abdominal wound, producing a complete gastric fistula. In certain animals, other fistulous openings were made in the intestine by attaching the cut edge of the intestine to the incision. In others a T tube was introduced into the intestine

3. Haden, R. L., and Orr, T. G.: The Effects of Sodium Chloride on the Chemical Changes in the Blood of the Dog After Pyloric and Intestinal Obstruction, J. Exper. Med. **38**:55-71 (July) 1923.

for the administration of fluids. A portion of the gastric wall was incorporated in the abdominal incision of one dog, and complete and partial gastrectomy, respectively, were performed on dogs as control experiments. In other dogs the proximal end of the duodenum was closed after complete or partial gastrectomy had been performed. Specimens of blood were obtained from the jugular vein at appropriate intervals, and the animals were kept in metabolism cages, urine and fistulous fluids being collected once in about twenty-four hours. The

TABLE 1.—*Chemical Changes in Blood, Urine and Fistulous Fluid of Dog with Gastric Fistula (Water by Duodenal Tube)*

		Blood		
Date, 1925	Hours Following Operation	Carbon Dioxide, per Cent by Volume	Urea Nitrogen, Mg. for Each 100 Cc.	Chloride, Mg. for Each 100 Cc.
3/3	0	67.1	9.9	633
3/4	22	85.5	16.6	561
3/4	31	57.4	20.2	608
3/5	48	85.5	28.2	466
3/5	56	96.5	28.4	425
3/6	72	108.4	36.4	410
3/7	97	106.3	48.7	330
3/8	126	94.7	60.1	311
3/9	144	102.3	61.4	220
3/9	152	103.3	45.3	239
3/10	168	109.9	30.0	209

		Urine				
Date, 1925	Specimen	Volume, Cc.	Period of Collection of Sample, Hours	Urea Nitrogen, Mg. in Total Sample	Ammonia Nitrogen, Mg. in Total Sample	Chloride, Mg. in Total Sample
3/3	1	40	7.5	668.4	10.0	200.8
3/4	2	250	16.5	1,670.0	580.0	1,478.5*
3/5	3	350	24.0	3,430.0	910.0	1,354.5*
3/6	4	260	24.0	1,374.0	650.0	661.4*
3/7	5	350	24.0	1,012.0	2,026.0	287.0*
3/9	6	900	48.0	3,276.0	3,024.0	1,986.0*
3/10	7	500	24.0	1,620.0	1,480.0	1,670.0*
		Fistulous Fluid*				
3/3	1	350	7.5	10.5	10.5	651.0
3/4	2	180	16.5	0.9	9.0	906.0
3/5	3	450	24.0	24.5	18.0	1,352.7
3/6	4	250	24.0	2.5	20.0	1,467.5
3/7	5	200	24.0	12.0	20.0	902.0

* The urine obtained by catheterization was added to that of the metabolism cage. The high chloride content is due to the mixture with the fistulous fluids. The fistulous fluid is only that which could be obtained without urinary contamination.

blood urea was determined by the method of Van Slyke and Cullen,[4] the carbon dioxide combining power of the blood plasma by the Van Slyke method,[5] and the blood plasma chlorides by the method of Whitehorn.[6]

4. Van Slyke, D. D., and Cullen, G. E.: A Permanent Preparation of Urease, and Its Use in the Determination of Urea, J. Biol. Chem. **19**:211-228, 1914.

5. Van Slyke, D. D., and Cullen, G. E.: I, The Bicarbonate Concentration of the Blood Plasma; Its Significance and Its Determination as a Measure of Acidosis, J. Biol. Chem. **30**:289-346 (June) 1917.

6. Whitehorn, J. C.: Simplified Method for the Determination of Chlorides in Blood or Plasma, J. Biol. Chem. **45**:449-460, 1920.

The urea content of the urine and fistulous fluids was determined by the method of Marshall [7] as modified by Van Slyke and Cullen.[8] The chlorides in the urine and fistulous fluids were determined by a slightly modified Volhard-Arnold method.[9]

CHANGES IN THE BLOOD

Following the production of experimental acute gastric fistula, the average rise of the carbon dioxide combining power of the blood plasma was 55 per cent by volume in animals receiving only moderate amounts of water by rectum and none intravenously. For example, in Dog H788 (chart 1, table 1), the carbon dioxide combining power of the blood rose within the first twenty-four hours after operation from a preopera-

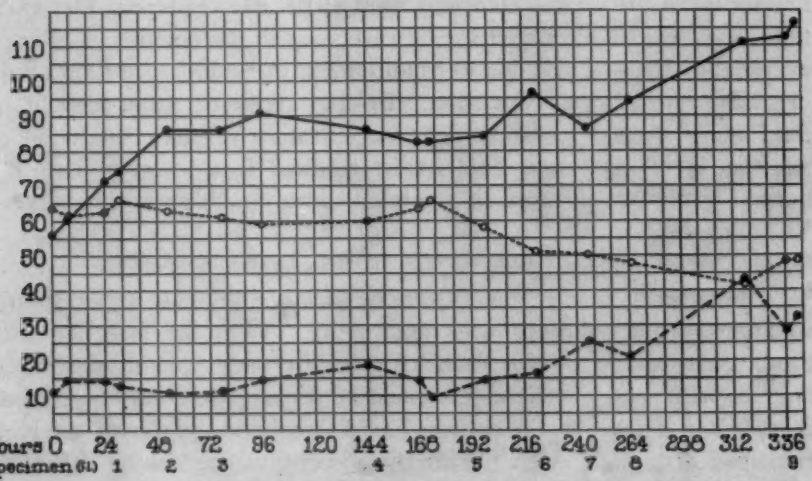


Chart 2.—Chemical changes in the blood in dog with gastric fistula following physiologic sodium chloride solution intravenously: solid dot solid line, carbon dioxide; solid dot broken line, urea; open dot broken line, chlorides.

tive level of 67.1 per cent by volume to 85.5 per cent by volume. Eight hours later, following the administration of fairly large amounts of water by duodenal tube, the carbon dioxide combining power was 57.4 per cent by volume. This rose within the next sixteen hours to 85.5 per cent by volume, and remained at this high level or above until it

7. Marshall, E. K.: A Rapid Clinical Method for the Estimation of Urea in Urine, J. Biol. Chem. **14**:283-290, 1913; The Determination of Urea in Urine, J. Biol. Chem. **15**:495-496, 1913; On Soy Bean Urease: The Effect of Dilution, Acids, Alkalis and Ethyl Alcohol, J. Biol. Chem. **17**:351-361, 1914.

8. Van Slyke, D. D., and Cullen, G. E.: A Permanent Preparation of Urease, and Its Use for Rapid and Accurate Determination of Urea, J. A. M. A. **62**: 1558-1559 (May 16) 1914.

9. Folin, Otto: Laboratory Manual of Biological Chemistry, with Supplement, ed. 3, New York, D. Appleton & Co., 1922.

increased to the maximum of 109.9 per cent by volume on the day of the dog's death. The decrease in plasma chlorides was equally striking. Within the first twenty-four hours after operation a decrease was noted, although some variations occurred within the first day or two. Following this period of adjustment, there was a progressive decrease until on the third day after the production of the fistula the chloride content was only two-thirds the normal amount. From this point, the decrease was continuously progressive so that only one-third the normal amount was present before the death of the animal. The changes in the urea nitrogen of the blood were somewhat more variable than those in the carbon dioxide combining power and the chloride content. In general, the urea content increased progressively and appeared to be greater when the plasma chlorides were at their lower levels. Its variations may be well accounted for by variations in the amount of nitrogen excreted by the kidneys, due to conditions in the kidneys, to fluid intake, or to the rate of urea formation. In dogs receiving small amounts of fluid there seemed to be a high concentration of urea in the blood, whereas increases in the fluid intake resulted in a lower level, and a normal level of blood urea was maintained only with great difficulty.

EFFECT OF SOLUTIONS GIVEN INTRAVENOUSLY

The effect of intravenous injections of large amounts of physiologic sodium chloride solutions was noteworthy. With the injection three times a day of 25 cc. for each kilogram of body weight, the life of animals with acute gastric fistula could be prolonged several days (chart 2, table 2). However, the carbon dioxide combining power of the blood remained at a high level. With the discontinuance of the injections, although a large quantity of water was supplied by mouth, characteristic changes in the blood recurred. Following the intravenous injections of comparable amounts of 5 per cent glucose solution, animals with gastric fistula appeared to be in slightly better condition than those receiving only water. There was less concentration of blood urea than in animals receiving water, and more concentration than in those receiving sodium chloride solution of similar tonicity. The decrease in the chlorides of the blood did not seem to be affected by the intravenous injections of glucose solution, as the decrease was the same as in the other animals except those to which chlorides were given. The increase in the carbon dioxide combining power of the blood was likewise not affected by the injection of this solution, since the rise was essentially the same in these animals as in the other untreated animals of the series. The life of the animals was maintained but little longer than that of those receiving water. Intravenous injections of 2 per cent sodium sulphate solution (25 cc. for each kilogram of body weight, three times a day) produced effects almost identical with those of glucose solutions of the same

tonicity (5 per cent). In these animals the urea of the blood continued to rise, the chloride content decreased, and the carbon dioxide combining power increased to the usual high level in animals with gastric fistula. The prolongation of life did not differ materially from that in animals receiving water or glucose solution intravenously.

TABLE 2.—*Effects of Physiologic Sodium Chloride Solution on Chemical Changes in Blood, Fistulous Fluid and Urine of Dog with Gastric Fistula*

		Blood			
Date, 1925	Time	Carbon Dioxide, per Cent by Volume	Urea Nitrogen, Mg. for Each 100 Cc.	Chloride, Mg. for Each 100 Cc.	Remarks
1/13	9:00 a. m.	55.5	10.10	638	Preoperative
1/13	3:50 p. m.	60.3	14.00	618	Injected 25 cc. 0.9 per cent sodium chloride for each kilogram
1/14	9:00 a. m.	71.9	14.14	627	Injected 25 cc. 0.9 per cent sodium
1/14	4:00 p. m.	74.8	12.82	660	chloride for each kilogram at 9:00, 1:30 and 4:00
1/15	2:30 p. m.	86.5	10.28	627	9:00 and 2:30, same injection; 4:30 injected same amount 0.6 per cent sodium chloride
1/16	3:30 p. m.	86.5	11.42	613	9:00 and 3:30, injection of 0.6 per cent sodium chloride
1/17	9:00 a. m.	91.4	14.81	592	9:00, injected 0.6 per cent; 3:30, injected 0.9 per cent
1/18	.....	....	.....	...	9:30, injected 0.9 per cent
1/19	9:30 a. m.	86.5	18.18	599	9:30, 2:30 and 4:30, injected 0.9 per cent sodium chloride
1/20	9:00 a. m.	82.6	14.70	635	9:00, injected 0.9 per cent sodium chloride
1/20	2:30 p. m.	82.6	9.90	658	600 cc. of water in rectum
1/21	4:15 p. m.	84.5	14.92	579	400 cc. of water in rectum
1/22	2:45 p. m.	96.5	16.80	519	400 cc. of water in rectum
1/23	2:30 p. m.	86.5	25.15	506	500 cc. of water in rectum
1/24	10:00 a. m.	94.2	21.62	486	Injected 25 cc. 0.9 per cent sodium chloride for each kilogram
1/26	2:00 p. m.	110.4	43.47	412	300 cc. of water in rectum
1/27	9:45 a. m.	111.6	27.10	486	Gastro-enterostomy performed
1/27	3:00 p. m.	116.8	32.47	486	

		Fistulous Fluid and Urine				
Date, 1925	Specimen	Volume, Cc.	Period of Collection of Sample, Hours	Urea Nitrogen, Mg. for Total Period	Ammonia Nitrogen, Mg. for Total Period	Chloride, Mg. for Total Period
1/14	1	1,000	26	2,707	143	4,620
1/15	2	1,200	24	2,570	955	6,550
1/16	3	950	24	150	290	6,100
1/19	4	1,600	72	8,592	5,168	7,648
1/21	5	750	36	2,400	2,700	3,697
1/22	6	950	30	1,700	380	2,480
1/23	7	1,250	24	2,300	2,060	3,887
1/24	8	950	20	494	114	636
1/27	9	1,300	72	1,960	2,210	1,560

The injection of a hypertonic solution of sodium chloride (5 per cent) maintained the chloride content at normal or slightly above, and also prevented a great rise in the urea content of the blood as well as the development of the typical conditions of alkalosis. The life of the animal was not prolonged, but even appeared to be somewhat shortened by the injection of this solution. The injection of hypertonic glucose solution (20 per cent) also failed to prolong the life of the animals, and did not alter the usual chemical changes in the blood.

EFFECTS OF TOTAL AND PARTIAL GASTRECTOMY

Total gastrectomy was performed on certain dogs, the esophageal and duodenal stumps being inverted as blind ends, and partial gastrectomy with gastrostomy on others. In the latter group practically the whole stomach was removed with the exception of a tube 20 cm. in length and 2 cm. in diameter. In the animals with total gastrectomy with

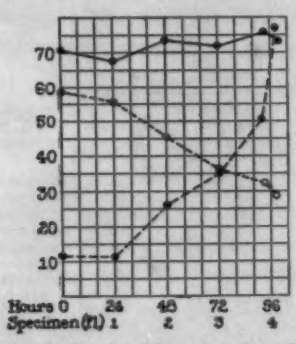


Chart 3.—Chemical changes in the blood in dog following total gastrectomy: solid dot solid line, carbon dioxide; solid dot broken line, urea; open dot broken line, chlorides.

TABLE 3.—*Chemical Changes in Blood and Urine of Dog with Total Gastrectomy (Water by Rectum)*

		Blood		
Date, 1925	Hours Following Operation	Carbon Dioxide, per Cent by Volume	Urea Nitrogen, Mg. for Each 100 Cc.	Chloride, Mg. for Each 100 Cc.
1/27	0	71.9	12.43	601
1/28	24	68.1	12.34	556
1/29	48	74.8	26.66	462
1/30	72	73.9	36.36	369
1/31	86	76.8	51.60	330
1/31	97	74.8	77.66	297

		Urine*				
Date, 1925	Specimen	Volume, Cc.	Period of Collection of Sample, Hours	Urea Nitrogen, Mg. for Total Period	Ammonia Nitrogen, Mg. for Total Period	Chloride, Mg. for Total Period
1/28	1	500	24	130	10	2,405
1/29	2	950	24	5,341	694	3,401
1/30	3	1,000	24	3,510	3,580	3,490
1/31	4	1,000	24	2,110	2,800	2,500

* Total fluids collected in metabolism cage.

inverted esophageal and duodenal ends, little change in the carbon dioxide combining power was noted for a period of four days (chart 3, table 3), thus further substantiating the hypothesis that the alkalosis or increase in the carbon dioxide combining power of the blood results from the loss of unneutralized acid through the gastric fistula. Again, in Dog H876 (chart 4, table 4) on whom partial gastrectomy with gastrostomy was performed as described and who received only water by rectum,

there was a rise in the carbon dioxide combining power of the blood plasma of only approximately 14 per cent by volume over a period of four days, a drop of the plasma chloride from 0.615 to 0.420, and but a moderate rise in the blood urea.

It would appear that the retention of alkali by animals with acute gastric fistula is quite similar to the milder degree of alkalosis that occurs in normal animals following the ingestion of food. The forma-

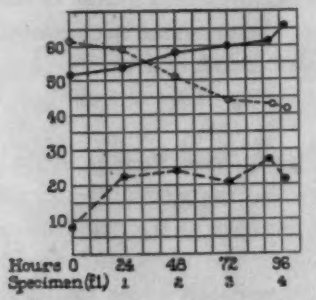


Chart 4.—Chemical changes in the blood in dog with gastric fistula following partial gastrectomy: solid dot solid line, carbon dioxide; solid dot broken line, urea; open dot broken line, chlorides.

TABLE 4.—*Chemical Changes in Blood, Urine and Fistulous Fluid of Dog with Partial Gastrectomy and Gastric Fistula (Water by Rectum)*

		Blood		
Date, 1925	Hours Following Operation	Carbon Dioxide, per Cent by Volume	Urea Nitrogen, Mg. for Each 100 Cc.	Chloride, Mg. for Each 100 Cc.
1/27	0	51.6	7.90	615
1/28	24	53.6	22.72	594
1/29	48	58.4	24.82	513
1/30	72	60.3	21.27	445
1/31	91	61.3	26.66	432
1/31	98	65.2	21.27	420

		Urine and Fistulous Fluid				
Date, 1925	Specimen	Volume, Cc.	Period of Collection of Sample, Hours	Urea Nitrogen, Mg. for Total Period	Ammonia Nitrogen, Mg. for Total Period	Chloride, Mg. for Total Period
1/28	1	420	24	411.6	105.0	651.0
1/29	2	250	24	1,752.0	160.0	295.0
1/30	3	500	24	2,165.0	1,315.0	1,290.0
1/31	4	600	24	2,514.0	870.0	1,580.0

tion of acid gastric juice from neutral compounds gives rise to the liberation of equal amounts of alkali which are retained in the body or excreted in the urine. However, even the most active digestive processes produce only a slight alkalosis as compared to that caused by gastric fistula. One might assume from this that the secretion of gastric juice is increased in animals with complete gastric fistula. Certainly there is an exceptional alkali retention in cases of gastric fistula which may be minimized by removal of the stomach or by loss of alkali from the intestine as in duodenal fistula.

In one experiment (chart 3, table 3) following complete gastrectomy with closure and inversion of the esophageal and duodenal stumps the concentration of the blood chlorides reached a minimal level of 297 mg. for each hundred cubic centimeters four days after operation, which would lead to the hypothesis that the reduction in blood chlorides is dependent on a mechanism other than the excretion by the stomach of the chlorine ion. It should be noted that 11.8 Gm. of chlorides were obtained in the fluid passed by rectum and in the urine of this animal during the postoperative life, evidence, we believe, that the reduction of blood chlorides may occur not only from the loss of secretion through the fistula but also as a result of their excretion into the lumen of the intestinal tract.

A study of the urea nitrogen content as well as the ammonia content of the fluids discharged from the gastric fistula and in the urine showed in general that with the increase in the blood nitrogen a similar increase in the nitrogen excreted in the urine and the fluids from the fistula frequently occurred. Immediately prior to death, the nitrogen lost in the fistulous fluids and urine suddenly decreased to a considerable extent, the result, we feel, of impending anuria and may be accounted for as a terminal event. It seemed reasonable that the increase in nitrogen was a result of its increased production. The cause of this increase in the production of urea is by no means certain, but since the oxidation of protein produces an acid residue it may be that the body is employing this means to neutralize the increasing amount of alkali in the tissues. This increase in the production of urea is less marked in those animals with less alkalosis, as is shown by the difference in urea formation in animals with gastric fistula and those with duodenal fistula. However, it should be pointed out that this increase in urea production is not prevented by the administration of salts other than sodium chloride.

In the dogs who had total gastrectomy with inverted esophageal and duodenal stumps (table 3) and also in the ones who had partial gastrectomy with gastrostomy (table 4), the amount of chlorides lost in the fluids of the fistula and urine was as much as, if not more than, that in the dogs who had gastric fistula with the stomach intact (table 1). This appears to be further evidence that the reduction in blood chlorides may occur not only from their loss in the gastric secretion through a fistula, but also as a result of their excretion into the lumen of the intestinal tract. The hypothesis of Haden and Orr [10] is that the loss of blood chlorides is due to their being given up to counteract the effects of toxemia resulting from interference in the motility of the gastrointestinal tract (chart 5).

---

10. Haden, R. L., and Orr, T. G.: Chemical Changes in the Blood of Man After Acute Intestinal Obstruction, Surg. Gynec. & Obst. **37**:465-468 (Oct.) 1923.

SUMMARY

Studies of complete acute gastric fistula in dogs have thrown light on several points. The chemical changes in the blood that occur are quite similar to those occurring in acute duodenal fistula and in high intestinal stasis. There is a marked increase in the carbon dioxide combining power of the blood plasma, an increase in the urea content of the blood, and a decrease in the chloride content. This increase in the carbon dioxide combining power of the blood plasma is much greater than that which occurs in the other conditions mentioned. Similar conditions, in the absence of the stomach or of the greater portion of the stomach, are attended by similar changes, with the exception that the carbon dioxide combining power of the blood remains within normal limits. These facts would make it appear that the alkalosis resulting from gastric fistula is due to a loss of acid from the stomach.

The administration to animals with gastric fistula of fluids other than physiologic sodium chloride solution serves to minimize the increase in the urea content of the blood but has little if any effect on the alkalosis or decrease in the chloride content of the blood. The administration of physiologic sodium chloride solution, however, tends to prevent any of these chemical changes from taking place and its use may greatly prolong the life of these animals.

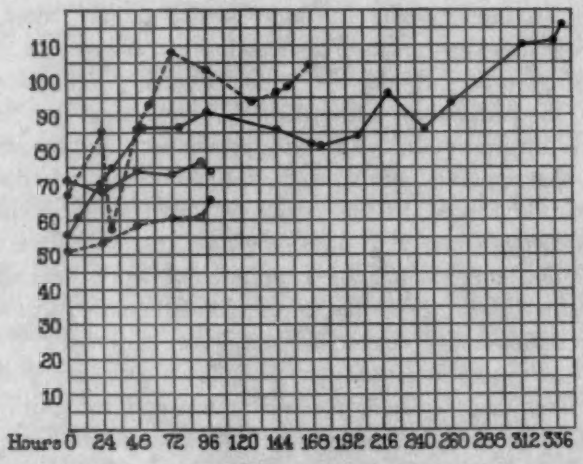


Chart 5.—Comparison of changes in carbon dioxide combining power of the blood in dogs under different conditions: open dot broken line, partial gastrectomy with gastric fistula; open dot solid line, total gastrectomy; solid dot solid line, gastric fistula—intravenous physiologic sodium chloride solution; solid dot broken line, gastric fistula—water by rectum.

POSTOPERATIVE GASEOUS DISTENTION OF THE INTESTINE

AN EXPERIMENTAL AND CLINICAL STUDY*

M. A. McIVER, M.D.
E. B. BENEDICT, M.D.
AND
J. W. CLINE, JR., M.D.
BOSTON

INTRODUCTION

Gaseous distention of the intestine is one of the most frequent complications following the trauma of abdominal operations, peritonitis or other type of injury to the abdominal viscera. It always entails discomfort to the patient and is sometimes a grave danger. The methods advocated in different clinics for its prevention and treatment are so varied in character and often in such striking contradiction to each other that one is forced to the conclusion that there is no general agreement as to the underlying physiologic processes. These processes are complex, and the amount of experimental work bearing directly on them is small. Some of the more fundamental features of the problem are undoubtedly concerned with the disturbances of motor activity of the gastro-intestinal tract, following injury. A clinical classification and discussion of the different types of injury will be found in articles by Murphy,[1] Rost [2] and others. The studies of Cannon and Murphy [3] should also be consulted: their experimental work deals with retarded intestinal mobility following various forms of injury, and they distinguish between direct injury to the local mechanisms in the wall of the intestine and other injuries that cause a reflex disturbance through the splanchnic nerves.

Although much has been written in regard to the motor effects of injury to the gastro-intestinal tract, many points remain obscure, and clinical articles on the subject of gaseous distention have often failed to make clear the fact that paralysis of the intestine does not per se

---

* From the surgical services, Massachusetts General Hospital, and the Laboratories of Physiology, Harvard Medical School.

* A preliminary note of this work appeared in the Boston M. & S. J. **192**:217 (Jan. 29) 1925.

1. Murphy, J. B.: J. A. M. A. **26**:15 (Jan. 4) 1896.
2. Rost, F.: The Pathological Physiology of Surgical Diseases, English Translation, Philadelphia, P. Blakiston's Son & Co., 1923, p. 212.
3. Cannon, W. B., and Murphy, F. T.: Ann. Surg. **43**:512, 1906; J. A. M. A. **49**:840 (Sept. 7) 1907.

cause such distention: the actual ballooning out must be brought about by positive pressure of gas within the lumen. The composition, origin and behavior of these gases are thus important features of the problem of distention.

Source of Gases of the Intestinal Tract.—The gases of the intestinal tract were first systematically studied by Planer [4] in 1860, and the work was later amplified by Ruge,[5] Tappeiner,[6] Tacke [7] and others. An extensive bibliography on the subject has been collected by Kantor.[8] The writers agree that the gases commonly present in intestinal meteorism are carbon dioxide, oxygen, nitrogen, hydrogen, methane and sometimes hydrogen sulphide, the proportions being subject to considerable variation. In considering the relation of these gases to distention, their origin must be taken into account.

One well recognized and important source for certain of the gases is found in the decomposition of intestinal contents. The work of early German writers, already mentioned, and the more recent studies by Boycott and Damant [9] furnish data on this subject and emphasize the influence of different types of diet on the kind of gas produced.

A second source is found in the diffusion of blood gases into the intestinal lumen. The walls of the intestine are permeable to gases, and an active interchange takes place, tending to keep the gases on the two sides of the intestinal mucosa in equilibrium. The mechanism of this exchange is discussed in detail in a report of our recent studies on the subject.[10]

A third, and less acknowledged, source for these intestinal gases must be considered. The gas normally found in the stomach consists primarily of atmospheric air, admitted by swallowing. Under conditions that will be described later, the amount of air is considerably increased, and we have come to believe that its passage downward into the intestine may be an important factor in the production of distention in certain cases. Articles by Ylppö [11] and Kantor [8] refer to this source of gas, and Beckham [12] mentions it as a factor in postoperative distention.

---

4. Planer, J.: Sitzungsb. d. k. Akad. d. Wissensch., Math.-naturw. Cl. **42**: 307, 1860.

5. Ruge, E.: Sitzungsb. d. k. Akad. d. Wissensch., Math.-naturw. Cl. **44**:739, 1861.

6. Tappeiner, H.: Ztschr. f. Physiol. Chem. **6**:432, 1882.

7. Tacke, B.: Ueber die Bedeutung der brennbaren Gase im tierischen Organismus, inaugural dissertation, Berlin, 1884.

8. Kantor, J. L.: Am. J. M. Sc. **155**:829 (June) 1918.

9. Boycott, A. E., and Damant, G. C. C.: J. Physiol. **36**:283, 1907.

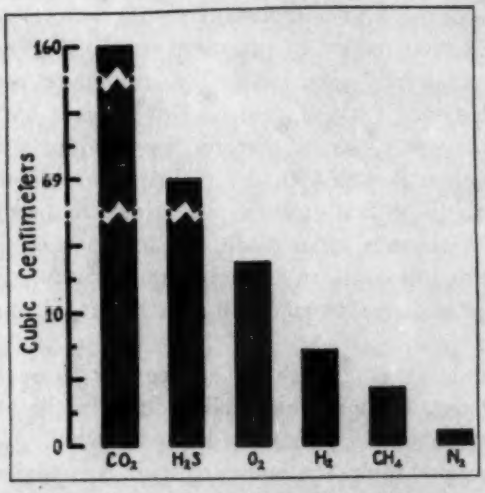
10. McIver, M. A.; Redfield, A. C., and Benedict, E. B.: Am. J. Physiol. **76**: 92, 1926.

11. Ylppö, A.: München. med. Wchnschr. **63**:1650, 1916.

12. Beckham, W. S.: Operative Surgery, Philadelphia, 1924, **1**:317.

In general, however, it has not received much attention in the literature, and little or no direct evidence has existed on which to judge its importance in the distention encountered in surgical practice.

The Body's Method of Eliminating Intestinal Gases.—The expulsion of gas by motor activity of the intestine is an important method of eliminating abnormal accumulations, and as stated above the interference with this mechanism which sometimes follows injury is a cardinal factor in distention. It is not, however, the sole method of eliminating gas. The diffusion of blood gases into the intestinal lumen was mentioned in a preceding paragraph; equally active is the reverse process, namely, the absorption of intestinal gases into the blood stream. Studies were recently carried out on this point by inject-



Relative rates of absorption, expressed in cubic centimeters, of carbon dioxide, hydrogen sulphide, oxygen, hydrogen, methane and nitrogen from a 25 cm. loop of the small intestine of the cat. The height of the columns represents the number of cubic centimeters of the gas absorbed over a period of one hour. In the case of carbon dioxide, because of the rapidity of its disappearance, and of hydrogen sulphide, because of its toxicity, the gas was withdrawn after the lapse of a few minutes, and the rate of absorption for one hour was calculated.

ing known quantities of the several gases into an isolated loop of intestine, leaving the gas for definite periods of time, withdrawing it, and determining the amount of absorption that had taken place. These experiments showed that while the rates of absorption vary greatly for the different gases, the amounts that can be eliminated by this mechanism are considerable. Figure 1, taken from a report [10] of this work, gives the relative rates of absorption of the gases commonly encountered in the intestinal tract. The height of the first column represents the amount of carbon dioxide, a gas liberated in great quantities when

fermentation is active, which can be eliminated in one hour from an isolated intestinal loop 25 cm. long. It is evident that the amount of this gas which could be absorbed in twenty-four hours from the intestine as a whole would be large. The next column represents hydrogen sulphide, a gas that is toxic to the organism, and this also is eliminated rapidly. The other gases represented show a slower rate of absorption; but it is obvious that any of them, with the exception of nitrogen,[13] could be eliminated in considerable quantities by this mechanism.

The rate of absorption of atmospheric air also was tested in these experiments, although the results are not shown in figure 1, and was found to be low, only 4 cc. being absorbed from a 45 cm. loop in five hours. This is to be expected, because of the close similarity between the composition of atmospheric air and that of the blood gases, and is of importance in connection with the view that air is a source of gas in distention.

Effect of Interference with the Circulation on Elimination of Intestinal Gases.—Since the absorption of intestinal gases by the blood stream is such an important method of elimination, it appears obvious that interference with the splanchnic circulation would upset this process and have serious consequences. It must be remembered, however, that there is little direct evidence where minor degrees of circulatory disturbance exist, and in the literature too much stress has been placed on this explanation for meteorism of obscure origin. The experiments of Kato,[14] who reported a slow absorption of carbon dioxide after ligation of the portal vein, and our own experiments on partial obstruction of this vein, represent too extreme a disturbance of the circulation to afford a useful comparison with clinical conditions, except in types of intestinal obstruction involving gross interference with the blood supply or in cases of thrombosis of the mesenteric veins.

Our experiments showed that if the veins to an empty intestinal loop are ligated, distention of the intestine by a bloody, fluid exudate will follow within a few hours,[15] owing to an increase in capillary

13. When 20 cc. of nitrogen are introduced into an empty intestinal loop, the absorption at the end of six hours is about 7 cc. If the same amount of nitrogen is introduced into an isolated loop in which digestion is in progress, at the end of the six hours the loop will be found greatly distended with gas. This is probably due to the fact that the abnormal presence of gas interferes with digestion and absorption and contributes to an active fermentation. This suggests that a vicious circle may be an important factor in marked degrees of distention, i. e., the presence of gas in an intestine in which digestion is in progress may result in increased fermentation and decreased absorption.

14. Kato, K.: Internat. Beitr. z. Path. u. Therap. d. Ehrnährungstör. **1**:315, 1910.

15. Murphy, F. T., and Vincent, B.: Boston M. & S. J. **165**:684, 1911. Murphy, F. T., and Brooks, Barney: Intestinal Obstruction, Arch. Int. Med. **15**: 392 (March) 1915.

pressure and damage caused by a poor supply of oxygen. If the intestinal loop is distended with air before the veins are obstructed, in addition to the fluid exudate, the volume of gas will increase, owing to a diffusion into the lumen of carbon dioxide from the blood.

PRESENT STUDIES

In a preceding paragraph, atmospheric air has been mentioned as a source of gas in intestinal distention. In the present studies an attempt has been made to estimate its importance in the distention following injury to the abdominal viscera. The work has consisted of animal experiments, supplemented by certain clinical studies.

Animal Experiments.—In order to determine some of the factors that govern the passage of air from the stomach into the intestine, certain animal experiments were carried out. These consisted of direct observations on the behavior of the stomach inflated with air. Additional experiments were carried out on the rôle of atmospheric air in the distention that accompanies general peritonitis. Abbreviated protocols illustrating salient features are appended.

METHOD

Cats, under chloralose anesthesia, were used in all these experiments. The observations were carried out in a moist chamber devised and described by Veach.[16] This piece of apparatus consists of a copper box large enough to receive a cat extended on an animal board; the bottom of the box contains water, warmed by an electric heating coil; the lid is supplied with glass windows for the purpose of observation, and small apertures permit the insertion of thermometer, tube from the tracheal cannula, etc.

After anesthetization, the animal was placed in the moist chamber, and the abdomen opened, the abdominal walls being held apart by ligatures attached to the sides of the box. From 60 to 90 cc. of air was introduced into the stomach, causing a moderate degree of distention; considerably more than this amount of gas is often encountered in the normal fasting stomach of the cat. In addition to observations on the course of events following this simple inflation of the stomach, the effects on the dilated stomach of stimulation or section of the splanchnic and vagus nerves were noted.

RESULTS

Effects of Simple Distention of the Stomach.—Vigorous peristaltic waves were usually set up following moderate inflation of the stomach. In certain experiments these continued for several hours without the

16. Veach, H. O.: Am. J. Physiol. **71**:229 (Jan.) 1925.

passage of gas from the stomach into the intestine; from time to time rhythmic activity of the small intestine and colon was observed. In other experiments, after a short period of gastric activity the small intestine and colon became distended, the stomach decreasing in size as the gas was passed into the lower intestinal tract (experiment 1). If the intestine is obstructed, gas will be passed down from the stomach and accumulate above the point of obstruction, and may there be drawn off (experiment 1). It is thus evident that during moderate distention the stomach is capable of passing gas into the lower intestinal tract.

Effects of Vagus and Splanchnic Section.—The splanchnic nerves were sectioned on the posterior abdominal wall shortly beyond their entrance into the abdominal cavity; the vagi were cut just below their entrance into the abdominal cavity, the dissection being carried around the esophagus down to the muscularis.

Following section of both splanchnic and vagus nerves, the motor activity of the stomach and intestinal tract was increased. Under this condition the gas was invariably passed from the stomach into the intestine. Experiment 2 is typical.

Effects of Vagus Stimulation.—Stimulation of both right and left vagi in the neck was carried out with the stomach distended by gas and resulted in great motor activity of the stomach and small intestine; but in no case was any gas observed to pass from the stomach to the intestine. This result was expected, since the increased tone and the contractions of the pylorus and duodenum would act as barriers to the passage of gas downward.

Effects of Splanchnic Stimulation.—When strong stimulation was applied to the splanchnics, major and minor, of the left side, just beyond their entrance into the abdominal cavity, increased tone in the stomach and an increase in peristaltic waves were noted in a number of cases. Under these conditions gas was passed down into the duodenum (experiment 3). Since this result was not abolished by cutting the splanchnic on the opposite side, and since the same result was obtained when stimulation was applied to the proximal, i. e., the spinal, end of the cut splanchnic, it would appear to be a reflex phenomenon transmitted through the vagi. When stimulation was applied to the distal end of the cut splanchnic (experiment 3), the typical inhibition of the movements of the stomach and intestine and the blanching due to constriction of the blood vessels, which were described by early observers, were noted. In certain cases during the increased activity following the period of inhibition gas was passed down. It is interesting that afferent impulses passing by way of the splanchnics are effective in causing a passage of gas from the stomach into the lower intestinal tract.

Effects of Peritonitis.—In addition to the experiments described above, certain others were carried out in order to determine whether by preventing the entrance of air from the stomach the occurrence of intestinal distention in general peritonitis might be prevented. The abdomen of the cat was opened, under ether anesthesia, and a massive peritoneal infection produced by the injection of a few cubic centimeters of colonic contents into the peritoneal cavity. In three of the six experiments at the time of this injection the pylorus was ligated. The abdomen was then closed. The animals quickly recovered from the immediate effects of the operation, but at the end of twenty-four hours showed systemic effects of the peritoneal infection. After twenty-eight hours, a lethal quantity of a barbituric acid derivative was administered and a necropsy performed.

The results were as follows: All the cats showed evidence of general peritonitis. The stomachs of all were dilated with gas. In the animals with pyloric obstruction, there was no distention of the small or the large intestine. In the animals in which no such obstruction had been produced, the findings were: One showed the stomach and upper 3 feet of small intestine distended; another, the stomach and upper three-quarters of small intestine distended; the third, the stomach and whole length of small intestine dilated. The colon was not dilated in any instance. Experiments 4 and 5 are typical.

These experiments suggest that atmospheric air is an important factor in the distention that accompanies general peritonitis; but they should not, of course, be construed as meaning that air is the sole source of gas. Fermentation of stagnating intestinal contents undoubtedly plays a rôle in most cases, and may at times be the most important source of gas.

CLINICAL STUDIES

The experiments described in the foregoing show that under certain conditions gas is passed down from the stomach to the intestine, and suggest that this may be one mechanism of intestinal distention. In order to see if any clinical confirmation of this view could be obtained, the following studies were carried out.

Gas Analyses from Postoperative Cases.—The first aspect taken up was the composition of the gases responsible for the distention encountered after operation. In table 1, analyses of gases from the patients in the surgical wards showing postoperative distention are presented, with additional analyses from distended cases in the medical wards for comparison. The data are not sufficiently complete to warrant detailed discussion; but attention is drawn to several points.

The gases found are the same as those identified by previous workers. In one instance only was hydrogen sulphide found to be present; it is

TABLE 1.—*Gas Analyses from Distended Patients in Surgical and in Medical Wards* *

Date	Diagnosis and Operation	Diet	Analysis of Gas: Carbon Dioxide	Oxygen	Nitrogen	Methane	Hydrogen	Hydrogen Sulphide	
3/11	Cholelithiasis (cholecystectomy)	Soft solids	4.0	4.2	88.0	1.7	2.1	..	
3/12	Cholelithiasis (cholecystectomy)	Liquids and soft solids	3.8	9.4	83.6	2.2	0.0	..	Postoperative patients in surgical wards
3/12	Retroversion of uterus (suspension and appendectomy)	Liquids	5.8	1.6	91.5	1.1	0.0	..	
4/ 9	Ventral hernia (repair of hernia)	Soft solids, but ate almost nothing	6.2	0.0	90.1	2.4	1.3	..	
5/20	Cholelithiasis (cholecystectomy)	Low residue	8.5	1.8	86.7	Combustible gases 3%			
2/16	Pneumonia	Soft solids	11.8	1.7	66.1	17.9	2.5	..	
2/20	Pneumonia	Soft solids	5.4	2.0	80.7	8.7	3.2	..	
2/19	Cardiac decompensation	Chiefly milk	7.5	1.3	54.8	3.3	33.1	..	
2/25	Cardiac decompensation	Chiefly milk	14.0	0 9	55.3	6.1	24.6	..	Patients in medical wards
2/27	Cardiac decompensation	Chiefly milk	9.6	1.6	49.2	5.3	34.3	..	
2/25	Diverticulitis	Soft solids, with milk	11.6	0.0	62.5	19.4	6.5	+	
2/20	Diarrhea	Soft solids	10.5	2.2	82.1	0.0	5.2	..	
3/12	For study	Milk and toast	5.1	1.1	89.1	1.3	3.4	..	

* The gases were collected under paraffin oil in a glass cylinder, by means of a rectal tube and a connecting tube which were also filled with oil. The gases were analyzed on a Haldane gas analyzer equipped with a combustion chamber. Lead acetate paper was used in testing for hydrogen sulphide.

probably rarely formed in large quantities and its absorption is rapid, as may be seen in the accompanying chart. The percentages of carbon dioxide, with a few exceptions, are close to those in venous blood, which is not surprising since this gas has a rapid rate of diffusion and is readily soluble in blood. The percentages of nitrogen are uniformly high, and since free nitrogen is liberated in the intestine only in small quantities if at all,[17] it must be derived from air: either directly, from swallowed air, or indirectly, by diffusion from the blood stream, which is saturated with nitrogen at four-fifths of an atmosphere of pressure. The oxygen figures are uniformly low. This probably means that the tension of this gas is low in the capillaries of the colon during distention, although a certain amount is used up in the process of fermentation. The percentages of hydrogen and methane are lower in the patients showing postoperative distention than in the medical cases, which suggests that fermentation was less active in the former; and since the composition (except for the small amounts of hydrogen and methane) is that of air modified by interchange with the blood gases, the findings are not inconsistent with the view that swallowed air plays a rôle in the production of postoperative distention.

Incidence of Gaseous Distention.—In order to form a basis for studies on the importance of atmospheric air in postoperative distention, an attempt was made to estimate the frequency with which this complication is encountered following abdominal operations. Very little information was found in the literature on this point (except in the work of Martzloff,[18] who discusses distention in relation to certain preoperative medication and will be referred to later) or as to the relative frequency following different types of surgical procedure. A study was therefore made of 107 cases in which a laparotomy had been performed. The classification of these cases, shown in table 2, is based on the anatomic site of the operation. Perhaps a more logical grouping would take into account the amount of trauma occasioned by the different operations and the degree of peritonitis present; but these points are so difficult to evaluate that it seemed safer to discuss the cases on a regional basis.

To determine the presence or absence of moderate degrees of distention is not an easy matter. The method used in making the present study was as follows: Immediately after operation, the appearance of the abdomen was noted and the circumference measured with a tape. For three or four days following the operation, longer if distention persisted, the patient was visited daily. It was found impossible to place great reliance on the measurements alone, especially when the changes

17. Krogh, A.: Skandin. Arch. f. Physiol. **18**:364, 1906.
18. Martzloff, K. H.: Bull. Johns Hopkins Hosp. **35**:370 (Nov.) 1924.

were slight; at the daily visits, therefore, in addition to the measurements the whole picture was taken into consideration: the appearance of the abdomen, the amount of tympany, etc. The results are given in table 2.

Of the 107 patients followed, thirty-six were considered to suffer from distention, although inevitably in a number of instances there might have been a difference of opinion by other observers, since in only a few cases was the distention severe. As will be noted, the patients who had undergone operations on the biliary tract showed the highest incidence of distention. The next highest incidence was found in the "pelvic cases," a group representing operations on the uterus and adnexa. The gastro-intestinal cases come next: a varied group involving operations on the stomach and duodenum, removal of the appendix, and so forth. The fourth or "miscellaneous" group consists chiefly of exploratory operations and operations on the kidney. Since hernia operations involve localized trauma to the peritoneum, twenty-nine patients were followed after operation; only one was distended.

TABLE 2.—*Classification in One Hundred and Seven Laparotomy Cases*

Biliary	Pelvic	Gastro-Intestinal	Miscellaneous
Total.....25	Total.....34	Total.....34	Total.....14
Distended.....12	Distended.....13	Distended..... 8	Distended..... 3

Total.....107
Distended..... 36

Additional Observations.—In addition to making the observations described above concerning distention, certain other points were noted, which for the sake of clearness were not included in table 2 but will now be briefly commented on.

The anesthetic employed, except in a few cases, was ether, preceded as a rule by nitrous oxide. The length of operation did not apparently influence the incidence of distention. In the majority of the cases the distention was apparent at the end of twenty-four hours. This agrees in general with the findings of Martzloff.[18] The usual duration was from forty-eight to seventy-two hours.

The subjective sensations of the patients also were recorded. The most important of these consisted of intermittent, shifting, cramplike pains which are usually referred to as "gas pains" but which do not necessarily imply any appreciable degree of gaseous distention. While most of our patients complaining of these pains did have a measurable distention of the abdomen, a number showed no visible evidence. About 50 per cent, for instance, of the patients of the first group shown in table 2 complained of "gas pains," and about the same percentage of the second group in table 3, although the incidence of distention was much

lower in the latter group. It is well known, also, that in the graver forms of distention, such as often accompany general peritonitis, while the patients may feel discomfort from distention, they do not suffer from "gas pains." It seems reasonable to suppose that this type of discomfort represents abnormal peristaltic activity of the intestinal tract, which, although usually associated with gas, may take place independently of any distention of the intestinal lumen.

Dilatation of the Stomach Following Operations.—Postoperative dilatation of the stomach is not uncommon. Leaving out of consideration the etiology of the most extreme form of this condition, known as acute dilatation, we find a number of causes for the presence of an unusual amount of air in the stomach after operation. It is, for example, well known that a great deal of air may be swallowed during the early stages of anesthetization: in three of the cases observed, 115, sixty-seven and fifty-four swallowing movements, respectively, were noted while the patients were being etherized. Again, it is a matter of common observation that great dryness of the mucous membrane of the mouth and pharynx is one of the after-effects of ether, and that many patients make an effort to relieve this by swallowing motions which carry air into the stomach. It was also observed that many of our patients following operation complained of gas in the stomach, which they often attempted to relieve by belching, and undoubtedly more air was swallowed in an attempt to relieve the gastric distress. A certain amount of air, also, is carried into the stomach at each swallowing motion when liquids are taken, and the exclusively liquid diet given after operation must be responsible for a considerable intake of air. It is also possible that during the retching which accompanies nausea and vomiting air may be gulped down.

Experiments with the Stomach Tube.—It has already been suggested that the air which is present in the stomach in unusual quantities after operation may be passed into the intestine and play an important part in intestinal distention. If this were true, it would seem possible that the incidence of this condition might be lessened by preventing the accumulation of air in the stomach. This supposition was tested in the following manner: While the patient was still under ether, a small stomach tube of the type advocated by Levin [19] was passed into the stomach through the nares. The gaseous contents of the stomach were then drawn off by means of a syringe; the tube was left in position for from twenty-four to forty-eight hours, and the gastric contents aspirated twice daily. The average amount of gas drawn off at the first aspiration was 145 cc.; the largest amount, 600 cc. In certain cases, in addi-

19. Levin, A. L.: J. A. M. A. **76**:1007 (April 9) 1921.

tion to the gas present there was an accumulation of fluid, the largest amount found being 480 cc., the usual amount much less.

In the group of cases in which this procedure was carried out, the incidence of distention was considerably reduced, as will be noted in table 3 in contrast to the group of cases shown in table 2 in which the procedure was not followed.

While the group thus tested was small, the more serious types of cases only were included, and the fact that the incidence of distention is low offers suggestive evidence that the passage of air from the stomach to the intestines does play an important part in the production of postoperative distention. Several clinical observations might be considered as in accordance with this idea. Was this mechanism, for example, in part responsible for the failure in preventing distention of the old preoperative regimen which included dietary restrictions and a free use of strong cathartics? Interesting, also, in this connection is the

TABLE 3.—*Cases in Which Stomach Tube Was Used*

Biliary	Pelvic	Gastro-Intestinal
Total.....11	Total..... 8	Total..... 6
Distended..... 2	Distended..... 0	Distended..... 1
	Total.....25	
	Distended..... 3	

effect of morphine after abdominal operations, for if fermentation due to inhibited motor activity of the intestine were the only source of gas, it might appear illogical to give a drug that would further inhibit peristalsis, and yet morphine is used liberally after abdominal operations and in the treatment of peritonitis, and the claim is made in many clinics that it has a tendency to prevent distention. (A census of clinics with reference to the use of morphine after operation has recently been made by Slocum [20].) Its beneficial effect may be explained in various ways, some of which will be touched on later; but among others it is suggested that by relieving gastric distress and diminishing reflex actions in general, morphine lessens the tendency to take air into the stomach, and by quieting gastric peristalsis it decreases the passage of air from the stomach into the intestine. It is also possible that the absorption of gas proceeds most rapidly from a quiet intestine.

TREATMENT

Certain points concerning treatment, some of them suggested by the foregoing studies, will be briefly discussed.

As regards the preoperative management of a case, the guiding principle should be to avoid as far as possible procedures that interfere

20. Slocum, M. A.: J. A. M. A. **84**:1264 (April 25) 1925.

with the normal functions of the intestine, and it should be remembered that this applies not only to the motor function but also to the absorbing function. It is obviously an advantage to have the stomach and small intestine empty and at rest at the time of operation; but a long starvation period is not necessary, since according to Alvarez [21] it requires only from seven to nine hours under normal conditions for the stomach and small intestine to become empty after a meal. In order that fermentation in the large intestine may be reduced to a minimum, it would seem logical to give a low residue diet during the day preceding operation. With the idea of further reducing fermentation in the colon, an enema on the morning of operation is frequently prescribed. Unless there is some special indication for this procedure, however, its wisdom may be open to question, for an important function of the colon is the dehydration of the contents received from the small intestine, and an enema often leaves a great deal of liquid feces which may result in more fermentation than if the normal condition had not been disturbed. The use of violent cathartics has been so universally abandoned that it does not seem necessary to touch further on this point; articles by Peet [22] and Alvarez and Taylor [23] cover the subject from both clinical and experimental points of view.

In the treatment after operation, one must of course be governed by the exigencies of the case; but it should be emphasized at this point that since rest is a fundamental principle in the treatment of injury, morphine, by quieting intestinal movements and preventing the spread of infection, provides the conditions most favorable for the recovery of the gastro-intestinal tract from the trauma of operation or other type of injury; and the relief from pain which it furnishes must be beneficial to the organism as a whole. Other modes of action by which morphine may prevent or relieve distention have already been suggested.

Consistent with the use of morphine to quiet intestinal movement is the policy at this clinic to avoid drugs such as pituitary extract and physostigmine, which are capable of setting up violent types of peristalsis. There may be occasional circumstances in which they are of use, and the arguments in their favor will be found in articles by Craig [24] and Martin and Weiss,[25] and also by Cross,[26] who has advocated a combination of the two. It is, however, interesting to note in this con-

---

21. Alvarez, W. C.: Surg. Gynec. Obst. **26**:651 (June) 1918.

22. Peet, M. M.: J. A. M. A. **71**:175 (July 20) 1918.

23. Alvarez, W. C., and Taylor, F. B.: J. Pharmacol. & Exper. Therap. **10** 365 (Nov.) 1917.

24. Craig, D. H.: New York M. J. **81**:527, 1905.

25. Martin, H. E., and Weiss, S.: Use of Physostigmine in Abdominal Distention, J. A. M. A. **84**:1407 (May 9) 1925.

26. Cross, D. G. T. K.: Brit. M. J. **1**:9 (Jan. 5) 1924.

nection that according to Martzloff,[18] in cases in which physostigmine (eserine) and strychnine were given before operation there was a higher incidence of distention than in those cases in which this treatment was not administered.

In the presence of distention of the colon, enemas often give relief. It is questionable whether their use should be pushed if they do not seem to produce this result. Hot applications to the abdomen, such as turpentine stupes or flaxseed poultices, especially when combined with the rectal tube, are unquestionably an important method of treating distention; it is probable, although there is no experimental evidence to support this view, that they stimulate a gentle, effective peristaltic action without setting up areas of localized contractions; and they may, perhaps, relax such contracted areas when these exist. It is also possible that they favor the absorption of gases from the intestine.

When we consider the influence of the postoperative diet, certain points might be mentioned. It is a generally accepted custom to use a liquid diet for a few days following abdominal operations. A theoretical objection might be raised to the use of milk during the period when distention is likely to occur, since it has been shown by the work of Ruge [5] that in the fermentation of milk a high percentage of hydrogen, a gas that is absorbed slowly, is liberated. As soon as circumstances permit, an ordinary diet should be resumed, since the intestine probably functions to best advantage under those conditions.

Our series of experiments showed that the small type of stomach tube, left in place for from twenty-four to forty-eight hours after operation, was of definite benefit in preventing distention. In the majority of instances the tube caused little or no discomfort to the patient and did not interfere in any way with the taking of nourishment. Since it is occasionally a source of annoyance to the patient, its use indiscriminately is not advocated; but in certain cases in which distention is feared as a grave complication it should be employed.

SUMMARY

1. The origin of the gases found in intestinal meteorism is threefold: the decomposition of intestinal contents; the diffusion of blood gases into the intestinal lumen through the mucosa, and the passage of atmospheric air from the stomach into the intestine. Absorption into the blood stream is an important method of eliminating intestinal gases. The rate at which absorption proceeds varies greatly for the different gases (discussed in text). The absorption of atmospheric air is slow, because of its similarity in composition to the blood gases, a point of importance in relation to air as a source of gas in distention.

2. Animal experiments showed that gas may be forced from the stomach into the lower intestinal tract by peristalsis or by increased gastric tone, thereby causing distention of the small intestine and colon. The increased motor activity from moderate distention of the stomach is at times sufficient to bring this about. Section of the extrinsic nerves (vagus and splanchnic) invariably resulted in increased activity and the passage of air downward. Afferent impulses by way of the splanchnics are also capable of producing this result.

The experiments on the distention accompanying general peritonitis suggest that atmospheric air is an important source of gas in these cases.

3. The validity of the supposition that air might be passed down from the stomach to the intestine, causing postoperative distention, was tested by preventing accumulations of air in the stomach through the use of the stomach tube. By this means the incidence of distention was considerably reduced, as shown in tables 2 and 3, suggesting that air may be an important source of gas in postoperative intestinal distention. Gas analyses from cases showing postoperative distention were consistent with this view.

4. Since rest is a fundamental principle in the treatment of injury, the quieting effect of morphine is beneficial and drugs such as physostigmine or pituitary extract which are capable of setting up violent types of peristalisis should usually be avoided. In cases in which serious distention is feared, the continuous use of a small stomach tube during the critical period should be considered.

PROTOCOLS

EXPERIMENT 1.—November 20; male cat; weight, 2 Kg. A small amount of milk was given the preceding night.

11:00: animal etherized; 9.5 cc. of chloralose given intravenously.

1:15: animal placed in moist chamber; abdomen opened. The stomach contained a small amount of gas; the small intestine and colon appeared flat. Peristaltic waves were noted over the stomach and coils of the small intestine.

1:30: 60 cc. of air introduced into stomach by syringe and needle.

2:10: dilatation of upper coils of small intestine noted; stomach appeared somewhat smaller.

2:25: stomach markedly decreased in size.

2:30: colon, which had been almost invisible, became dilated. Needle introduced and 30 cc. of gas drawn off from stomach, completely emptying it.

2:40: the gas was milked out of upper part of small intestine, and a needle with rubber tube attached was inserted about 30 cm. from pylorus and held in place by a silk ligature around the intestine. The rubber tube, previously filled with water, was carried under a test tube filled with water and immersed in a beaker of water. Ninety cubic centimeters of air was introduced into stomach; complete inhibition of all movements of stomach and intestine followed.

4:27: peristaltic waves again noted passing over pyloric portion of stomach.

4:55: peristalsis very active over stomach and upper part of small intestine. Small intestine appeared gas-containing, gas being pushed by peristalsis almost to the point of obstruction.

5:10: gas bubbled through needle and rubber tubing and was collected in the test tube under water.

EXPERIMENT 2.—November 22; female cat; weight, 2.2 Kg. No food for twenty-four hours.,

9:50: light ether; 12 cc. of chloralose injected intravenously.

11:30: animal placed in moist chamber; abdomen opened. Stomach small in size; small intestine and colon collapsed. Vigorous peristalsis over stomach and in certain coils of small intestine.

11:35: 60 cc. of air introduced into stomach.

12:05: deep waves passing over stomach, but no gas has entered duodenum.

12:15-12:24: right and left splanchnics, major and minor, divided. Vigorous peristalsis noted over small intestine and stomach. Moderately deep waves over cardiac portion, but this did not extend down over the antrum pylorus. While tone over stomach appeared marked, peristaltic waves were disordered and passed over stomach in disorderly fashion, making it appear as though the gas were being churned up and down. No gas was discharged into small intestine.

12:50: right and left vagi cut, just above cardia.

1:00: deep peristaltic waves passing over entire stomach at rate of 8 per minute.

1:10: duodenum dilated.

2:30: duodenum and upper coils of small intestine distended with gas.

EXPERIMENT 3.—January 12; female cat; weight, 2 Kg. No food for twenty-four hours.

10:20: ether started; 8 cc. of chloralose given intravenously.

11:00: light ether, while tracheal cannula was inserted.

12:00: animal light; additional 2 cc. of chloralose given.

12:45: animal placed in moist chamber. Abdomen opened.

1:00: left splanchnics, major and minor, isolated, and guarded electrode, connected with an inductorium, applied to the nerves.

1:15: moderately strong stimulation applied for one and one-half minutes. Great blanching of blood vessels of stomach and intestine noted. Tonus rings appeared over pyloric portion of stomach, but no air descended.

1:20: irregular peristaltic waves observed over cardiac portion of stomach.

1:25: splanchnic stimulated for one and one-half minutes. Great increase in stomach tone, with deep peristaltic waves. Air forced into duodenum during and following this stimulation.

2:45: left splanchnic divided, between ligatures.

3:00: stimulation of distal end of cut splanchnic for one minute. Blanching of blood vessels and inhibition of stomach activity noted. Return of gastric activity a few minutes after stimulation stopped. During this time a small amount of air entered duodenum.

3:25: electrodes applied to proximal end of cut splanchnic.

3:27: stimulation for one minute.

3:30: right splanchnic cut.

3:45: stimulation of proximal (spinal) end of left splanchnic. Increase in gastric tone and deep tonus waves noted. Duodenum distended by gas which was observed entering from the stomach.

EXPERIMENT 4.—June 16; weight, 3.5 Kg. Had access to water, but no food for twenty-four hours.

Abdomen opened under ether anesthesia; stomach contained usual amount of air (estimated 50 cc.); small intestine and colon flat.

Portion of omentum resected. A needle introduced into the colon and about 1 cc. of semifluid material drawn into syringe. Diluted with water to 5 cc. and injected into peritoneal cavity.

June 17: cat listless, not inclined to move about.

June 18: cat looked sick and listless, and had vomited several times. A lethal dose of a barbituric acid derivative was administered.

Necropsy: abdomen opened; purulent peritonitis present. Stomach dilated with gas; upper three-fourths of small intestine distended with gas; colon flat.

EXPERIMENT 5.—June 16; weight, 2.3 Kg. Had access to water but no food for twenty-four hours.

Abdomen opened under ether anesthesia; stomach and intestine empty. A portion of omentum resected and peritoneal cavity infected as in preceding experiment.

Pylorus ligated.

June 17: general appearance indicated severe infection; had vomited once.

June 18: general condition appeared worse; very drowsy and listless. A lethal dose of a barbituric acid derivative was administered.

Necropsy showed purulent peritonitis. Stomach greatly dilated with gas. Small intestine empty except for a small amount of bile stained fluid. Colon empty.

THIRTIETH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY*

ROBERT B. OSGOOD, M.D.; NATHANIEL ALLISON, M.D.
PHILIP D. WILSON, M.D.; HERMAN BUCHOLZ, M.D.
ROBERT SOUTTER, M.D.; HARRY C. LOW, M.D.
MURRAY S. DANFORTH, M.D.
LORING T. SWAIM, M.D.
AND
M. N. SMITH-PETERSEN, M.D.
BOSTON

(Concluded from page 458)

PERIPHERAL NERVE SURGERY

Nerve Anastomosis.—Ballance, Colledge and Bailey [32] have made an experimental study of various methods of nerve anastomosis. They conclude that with sutures of absorbable material it is unimportant whether the suture passes through the neurolemma alone or whether it penetrates the nerve substance. Varnishes were tried as a substitute for sutures, but the only one that was at all successful was that made by cutting a piece of living muscle into fine bits and pounding this up with a few drops of salt solution in a mortar so that sarcous material was set free. Anastomosis by the method of double lateral implantation was successful if the ends were placed not too far apart. When a median incision is made in the receiving nerve the tendency is for the two ends to become connected. Exact end-to-end suture of the nerve fibers is not possible in any case.

Traumatic Neuritis of the Ulnar Nerve.—Platt [33] has made a thorough study of the pathogenesis and treatment of traumatic neuritis of the ulnar nerve in the postcondylar groove of the humerus. He points out that normally the nerve is mobile in this situation and may even be hypermobile. The condition is discussed under three headings: first, fracture of the lower end of the humerus with early involvement; second, late involvement; third, recurring dislocation of the nerve from its bed. Of 329 cases of fracture of the region of the elbow treated by Platt, involvement of the ulnar nerve was encountered in only nine cases. All of these occurred in fractures of the humerus and eight were in fractures of the internal condyle. Seven of these patients recovered spontaneously in from three to eight months. In 600 operations on the

32. Ballance, C.; Colledge, L., and Bailey, L.: Brit. J. Surg. **13**:533 (Jan.) 1926.

33. Platt, Harry: Brit. J. Surg. **13**:409 (Jan.) 1926.

peripheral nerves there were only two in which the ulnar nerve was found encased in callus. The nerve bed was often found to be altered, however, in such a way as to produce pressure or friction. Early involvement of the nerve is rare (nine out of 252 cases) and occurs most commonly in conjunction with fracture of the internal condyle. It is usually due to the primary contusion of the injury and tends to get well. Operation is indicated only after failure to improve at the end of a considerable period. When the symptoms develop after a latent period, the involvement is due to an alteration in the nerve bed, and operative treatment is usually necessary. Late involvement may occur as a remote sequel of fracture of the external condyle in childhood, and is due to friction or tension of the nerve. This condition necessitates operative treatment, either anterior transplantation of the nerve or correction of deformity by supracondylar osteotomy. Recurring dislocation of the nerve from its bed is due to a change in the configuration of the postcondylar groove, and transplantation of the nerve to the front of the elbow is indicated.

Periarterial Sympathectomy: An Easy and Rapid Method.—Camera [34] has devised a technic to obviate some of the difficulties of periarterial sympathectomy by the usual method. After isolating the artery and lifting it on a hook, he introduces a long slender needle into the vessel wall and passes this downward between the superficial and muscular coats for its entire length. He then slowly injects sodium citrate solution, withdrawing the needle as the injection is made. By this means the adventitia is distended and separated from the inner layers and can then be readily stripped away by scissors or scalpel dissection. He reports that Leriche has used this method since it was called to his attention and seemingly finds it helpful.

Effect of Periarterial Sympathectomy of the Renal Artery.—Melzner [35] has done periarterial sympathectomy on the renal artery in dogs, but was unable to perceive the slightest histologic change in the kidney after an interval of from three to seventy days. From his experiments he concludes that there is a segmental arrangement of the nerve supply of the vessels and that the operation of periarterial sympathectomy in general produces no marked effect on the circulation.

Operations on the Peripheral Nerves as a Substitute for Periarterial Sympathectomy.—As sympathectomy is not without risks and is attended by conflicting and irregular results there is a beginning tendency to turn to the peripheral nerves and to attempt to obtain vasodilatation by means of various procedures applied directly to them. Thus

34. Camera, Ugo: Chir. d. org. di movimento **10**:195 (Dec.) 1925.

35. Melzner, E.: Arch. f. klin. Chir. **136**:427, 1925.

Taylor and Rice [36] have exposed the sciatic nerve and injected it with 15 per cent alcohol solution. They have employed this procedure in twelve patients, ranging in age from 9 to 70 years. In all the cases treated, vasodilatation of the corresponding foot and lower third of the leg developed, as shown by flushing and hyperthermia of the parts. Hyperthermia may be produced without paralysis by this method, but the degree of hyperthermia is proportional to the degree of nerve interruption, that is, to the degree of paralysis produced. They regard this method as far more reliable than periarterial sympathectomy to obtain hyperthermia. The indications for this procedure are stated to be the same as those for sympathectomy. It is not of value in arteriosclerotic gangrene and Buerger's disease.

Stretching the Sciatic Nerve.—Bertone [37] has employed forcible traction of the sciatic nerve under deep anesthesia to obtain the same effects as did the authors of the previous article by alcohol injection. He regards this procedure as much surer and safer than periarterial sympathectomy. It was used by his chief, Giordano, as early as 1894. In his clinic at Venedig he has thus far treated 100 patients by the method with good result.

Diez [38] has also approached the problem from a similar angle. When the condition to be treated affects the hand he exposes the median nerve, incises the sheath, and separates the nerve fibers into from twelve to fifteen bundles; when it affects the leg he separates the sciatic nerve into from thirty to forty bundles. The interfascicular tissue is removed and the sheath is then closed with a few fine stitches. Following the operation there are noted in the extremity hyperemia, a rise of the arterial blood pressure and of the oscillimetric index. So far the operation has been performed in thirteen cases of obliterative endarteritis and in eight cases of Raynaud's disease, with results that are considered satisfactory.

[Ed. Note.—Few operations so questionable from an anatomic and physiologic standpoint have had so wide a popularity as periarterial sympathectomy. It has been developed as a cure-all by enthusiasts, the conditions treated varying from the circulatory disorders for which it was originally advocated to ununited fractures, leprosy, syphilis, and bone and joint tuberculosis. It has been necessary to wait a certain time before trying to arrive at a just estimate of the value of the procedure. It seems to have been established that the operation produces certain characteristic reactions in the extremity, consisting of hyperemia

36. Taylor, K. P. A., and Rice, J. B.: Injection of Sciatic Nerve as Substitute for Femoral Periarterial Sympathectomy, J. A. M. A. **86**:191 (Jan. 16) 1926.

37. Bertone, K.: Zentralbl. f. Chir. **52**:2248 (Oct. 3) 1925.

38. Diez, Julio: Arch. de la conferencia de med. del hop. Ramos Mejia **8**:130, 1924.

and hyperthermia, which last for from seven to fourteen days. Ulcers and wounds are stimulated to heal, and pain from circulatory deficiency is relieved. That any permanent benefit results has not been established, nor have impartial observers noted any real improvement in cases of thrombo-angitis obliterans or in obstruction due to arteriosclerosis. In addition, the operation is not without risk, as shown by the report of several disasters. We are of the impression that less will be heard of this operation as time goes on, and we would hesitate to recommend it ourselves in any but exceptional conditions. As the effort to find a substitute for periarterial sympathectomy in operations on the nerves, this is to be encouraged, but the work should be done in the laboratory on animal subjects under proper control. We cannot too strongly condemn the trial of surgical innovations on human patients when their value can be determined by animal experimentation.]

FRACTURES

The Value of a Fracture Service in Hospital Organization.—Scudder [39] emphasizes the necessity of making individual surgeons responsible for the care of each fracture case from the accident ward, through the period of hospitalization down to and including the period of convalescence when the patient is under treatment in the outpatient department. In the later stages the social service worker is most important in bringing about a spirit of cooperation that is entirely lacking in most of our hospitals today. The work of the whole fracture organization has but a single object, that of getting the man back on his job. Standardized equipment and a trained personnel are needed. A special fracture service provides better opportunities for treatment and helps to raise the standards of treatment in general practice.

Fractures About the Elbow Joint.—Ritter, Basher, Wurtzel and Goldblatt [40] conclude from a study of 150 cases of fracture about the elbow with known end-results in fifty-two cases that the results obtained in the treatment of these injuries are often most unsatisfactory from the standpoint of both function and deformity, although failure of union almost never occurs. They have nothing new to suggest in the way of treatment, contenting themselves with the stereotyped formula that with the exception of fracture of the olecranon the patients should all be treated with the elbow fully flexed and the forearm supinated. They emphasize the need of proper reduction, which is to be accomplished by complete flexion of the elbow with downward traction on the

39. Scudder, C. L.: Bull. Am. Coll. Surgeons, Jan., 1926, p. 32.

40. Ritter, H. H.; Basher, W. W.; Wurtzel, G. L., and Goldblatt, Davis: Fractures About the Elbow Joint, J. A. M. A. **86**:680 (March 6) 1926.

forearm. They feel that early functional restoration is dependent on early motion and massage.

[ED. NOTE.—We feel that improvement in results may be obtained in many of the elbow fractures by more frequent resort to the open method. Only by this means can complete reposition of fragments be secured in the comminuted intra-articular fractures and if they are fixed securely by internal splints movement and massage may be begun at once.]

End-Results in Fractures of the Femur.—Ashhurst and Crossan [41] have made a study of 111 consecutive fractures of the femur. Of the ninety-eight patients who survived their injuries, eighty-seven, or 89 per cent, were traced. Among these eighty-seven patients, anatomic reposition of the fragments was secured in forty-four, or 50 per cent. Moderately accurate reduction was obtained in thirty-four, or 40 per cent, and in nine only was the position of the fragments bad at the time of consolidation. Fifty-five patients, or 63 per cent, had no functional disability whatever; twenty-six, or 30 per cent, had moderate functional disability, and only six, or 7 per cent, were incapacitated. Nearly 64 per cent of the patients returned to work in less than six months; nearly 84 per cent returned in less than nine months. For fractures through the neck and trochanters, either the abduction cast was used or the patient was treated as for fracture of the shaft of the femur, the choice depending on the level of the fracture and the best method of overcoming the deformity. For fractures of the shaft and most supracondylar and intercondylar fractures, Buck's extension was employed, with the patient's leg resting on a sliding splint to overcome friction. Operation was employed in 9 per cent of the cases, and less often in recent years than formerly—only three times in the last eight years.

Fractures of the Ankle.—Platt,[42] writing on fractures of the ankle, follows Ashhurst's method of classifying them according to mechanism into fractures by external rotation, by abduction, and by adduction. He advises closed methods of treatment for fractures with a small amount of displacement. Out of 116 cases the open method was employed in only four. His study of end-results showed increasingly good functional results in 90 per cent after two years.

Ununited Fractures.—Henderson [43] has made a study of 259 cases of ununited fracture that were treated at the Mayo Clinic in the last

41. Ashhurst, A. P. C., and Crossan, E. T.: Prognosis and Treatment of Fractures About the Elbow Joint, J. A. M. A. **86**:680 (March 6) 1926.

42. Platt, Harry: Fractures in the Neighborhood of the Ankle Joint, Lancet **1**:33 (Jan. 2) 1926.

43. Henderson, M. S.: Ununited Fractures, J. A. M. A. **86**:81 (Jan. 9) 1926.

six years. These were divided on an arbitrary basis into ninety-six cases of delayed union and 163 cases of nonunion. Included in the latter group were twenty-eight cases of ununited fracture of the hip, the results in which are considered separately. All of the 259 patients were treated surgically, the operative procedures being classified either as bone grafts or plastic operations. For grafting purposes usually the massive type of graft was employed. Plastic operation was the term applied to any procedure in which the fragments were shaped and fitted to each other and fixed by various means but without the use of a graft. A bone grafting operation was done in forty-three cases of delayed union and resulted in a cure in forty of the forty-two patients traced (96.2 per cent). Of the 163 cases of nonunion, the bone graft was used in 104, with cure in eighty-one of the ninety-eight cases traced (82.6 per cent). In the combined group the bone graft produced a cure in 86.4 per cent of the patients treated. In twenty-two cases of nonunion of the hip, bone grafts were used, usually from the fibula, and bony union resulted in sixteen of the twenty-one patients who were followed. Plastic operations in one form or another were performed in fifty-five cases, exclusive of the hip, thirty-two being classified as delayed union and twenty-three as nonunion. Cure resulted in 93 per cent of the cases of delayed union, but in only 65 per cent of those with nonunion. Five of the patients with nonunion of the hip were not considered suitable for bone grafting and they were subjected to the plastic operations of either Whitman or Brackett. Satisfactory results were obtained in all. The cases were carefully studied from the standpoint of etiology, and the outstanding factor appeared to be severe direct injury, so severe that there was no question as to its importance in the devitalization of the tissues. Sixty-two of these severe injuries were associated with compound fractures and fifty-six with simple fractures. Forty-seven compound fractures were encountered in the cases of nonunion, whereas only fifteen were in the delayed union group, showing that severe injuries with compound fracture are prone to lead to nonunion. A severe injury with a simple fracture appeared responsible in fifty-six of the cases. Inadequate fixation appeared to be responsible in twenty-three cases; poor reduction, with or without interposition of tissue, in forty cases; the presence of metal fixative material in eleven cases, and in thirty-nine cases no cause could be determined. Determination of the calcium and phosphorus content of the serum was made in practically all of the cases, but with indefinite results. The fact that a higher percentage of cures was obtained by both methods in the cases of delayed union, 93 per cent as compared with 73.8 per cent in the nonunions, leads him to conclude that the earlier an incipient nonunion is recognized and treated, the greater will be the chance of cure.

[ED. NOTE.—Henderson's report based on a large series of carefully studied and followed cases establishes a standard by which the prognosis in cases of ununited fractures can be estimated. His percentage of cures is extraordinarily high.]

RESEARCH

The Influence of Surgical Disease on the Development of Nuclei of Ossification.—Buonsanti [44] has studied the carpal bones, basing his conclusion as to the normal time for appearance of the various nuclei on the work of Alberti, Busi and Weil. The object of his study is to ascertain what relationship disease has to the development of these centers of ossification. He has divided the significant diseases in six classes: (1) tuberculosis of the glands and of distant bony segments; (2) tuberculosis near the carpus; (3) acute inflammatory diseases; (4) constitutional disease; (5) tumors; (6) congenital and acquired deformities. He believes that sex influences the development, as females show earlier ossification, but ossification is variable within the normal limits of one to three years. He has found that neither distant nor neighboring disease has any influence on ossification. Constitutional disease and deformity also do not influence the development of the nuclei. Likewise, the application of dressings and splints does not affect the appearance of centers of ossification. His study is based entirely on roentgenograms.

Acute Bone Atrophy.—Noble and Hauser [45] have studied a condition described by them as reflex trophoneurotic atrophy of the bone. This condition arises in injured and diseased bones, frequently after slight injury, such as Colles' fracture. The bones rapidly atrophy, with pain as the characteristic symptom. The roentgenograms show calcium salts in the soft tissues. The authors believe that the lymph flow from the distal part of the extremity carries away the calcium from the bones and deposits it in the soft parts; pain results from calcium salts in the tissues. Treatment for the acute trophoneurotic atrophy consists of radiant heat, massage and voluntary motion in spite of pain. Fixation is contraindicated.

[ED. NOTE.—We feel that Noble and Hauser have failed to justify many of their conclusions. It has long been admitted that acute atrophy of the bone suggests a neurologic factor associated with the ever present atrophy of nonuse. It seems, however, that other steps than the study of roentgenograms must be taken to establish this factor as a cause. Also it seems that the assumption that the lymph circulation carries away the bone salts is unwarranted.]

---

44. Buonsanti, Paolo: Chir. d. org. di movimento **10**:61 (Dec.) 1925.

45. Noble, T. P., and Hauser, E. D. W.: Acute Bone Atrophy, Arch. Surg. **12**:75 (Jan.) 1926.

The Dangerous Period in the Development of the Hip Joint.—Harrenstein [46] believes that unfavorable mechanical conditions at the hip during the later months of pregnancy may bring about dislocation of the hip before the birth of the child. He has examined ninety-five pelves of fetuses, new-born babies and adults, and believes that the depth of the pelvis is least during the period when the length of the body is from 36 to 60 cm.; that the female pelvis is shallower than the male, explaining the greater frequency of dislocation in the female; that the left acetabulum is shallower than the right, explaining the greater frequency of left dislocation. LeDamany has found that in France the right acetabulum is deeper than the left; this differs from the reports from England, Germany and Austria. The female acetabulum is more sagittal and vertical than the male. He emphasizes the fact that during the 36 to 60 cm. period of fetal development the posture of the fetus is favorable to subluxation at the hip.

The Question of Reunion of Osteochondritic Joint Mice.—Lehmann,[47] in observing a series of early, not yet fully separated osteochondritic, potential joint mice, has found not only pseudarthritic processes, but also bridges between the subchondral tissue, and the osteochondritic area, suggesting that complete reconstruction is possible.

The Changes in Metabolism Associated with Fracture.—Dannheiser [48] has checked the work of Rehns on the muscle reaction to electricity in fracture of the bones. In the first week the muscles show decreased irritability, so-called stupor. In the following four weeks there is gradually increasing irritability, approaching the tetanic state. After four weeks the muscles gradually return to normal. The urine is acid for from six to twelve days, then alkaline for about a week, returning to normal thereafter. The hydrogen ion concentration in the urine was found to be similar to the findings of Rehns.

The Vertebral Column from the Anatomic and Physiologic Standpoints.—Gallois and Japiot [49] have observed that the vertebrae have an internal architecture following a perfectly definite rule. The bony lines follow practically the rules laid down by Julius Wolff in his description of the neck of the femur and the os calcis. The lines of bone are vertical, oblique and horizontal, and form two systems of support, a principal and an accessory. The principal lines of support are vertical. These lines exist in all the vertebral bodies and follow in line as if the intervertebral disks did not exist. They begin at the axis and extend to the sacrum. This gives a unity in the vertebral column and an indi-

46. Harrenstein, R. J.: Ztschr. f. orthop. Chir. **46**:481, 1925.
47. Lehmann, J. C.: Deutsche Ztschr. f. Chir. **88**:192, 1925.
48. Dannheiser, F.: Arch. f. klin. Chir. **136**:292, 1925.
49. Gallois and Japiot: Rev. de Chir. **63**:688, 1925.

viduality to each vertebra. The accessory system of support unites the body of the vertebrae by oblique and horizontal lines, two superior and two inferior. From the rectangular point of view, the vertebra is divided into two parts, a massive body and the apothesis. The bodies are supportive and the apotheses are the levers that control them by means of the muscles. The architecture of the different parts of the vertebrae corresponds to the laws established by Culman for the neck of the femur. The architecture of the vertebrae seems to be planned for two purposes: (1) to resist compression and (2) to permit the control of motion by the apotheses without lessening the supportive quality of the spine and without injury to the spinal cord and the nerves coming from it.

Experimental Research on the Regeneration of Articular Cartilage.—Haebler,[50] using dogs, has performed twenty-two experiments, the purpose of which was to determine the healing power of articular cartilage. When the cartilage alone was injured without injury to the subchondral bone, the wound in the cartilage showed no change after 300 days, showing that the cartilage itself has no power of regeneration. When the subchondral bone is injured as well as the cartilage, the cartilage defect is filled with fibrous tissue. The cartilage beyond the area of injury remains normal. He found that altered function of the joint, such as is produced by amputation, plaster-of-paris, or other lesion, results in arthritic changes in the cartilage.

MISCELLANEOUS

Lumbarization of the First Sacral Vertebra and Spondylolisthesis.—Léri [51] gives such an excellent diagnostic symptomatology of the lumbarization of the first sacral vertebra and its forward slipping that it is worth reporting. He considers the clinical picture very characteristic. The onset of the trouble is often attributed to a definite trauma, such as a fall from a horse or a ladder. Even before the roentgenogram is studied the stance of the patient is suggestive. Some lateral deviation of the spine may often be observed and the sacrum is more prominent. The examining finger will feel a marked depression at the fifth lumbar vertebra. The shoulders are squared. The waist appears shortened and the abdomen more prominent. The lower part of the spinal column is farther forward than normal. When the patient bends backward the lumbar angle is increased, and when he leans forward this angle does not entirely disappear, and no normal lumbar kyphos is produced. Most of the motion in the spine is dorsolumbar instead of lumbar. The walk often suggests a waddle. The pain, which has often

50. Haebler, C.: Beitr. z. klin. Chir. **134**, 1925.

51. Léri, André: Presse méd. **332**:1681 (Dec. 23) 1925.

existed for years, is usually nagging rather than intense and is felt in the region of the lumbosacral junction medially or laterally. As a rule, it does not radiate along the nerves and may resemble that of Pott's disease. It is not relieved by sitting, but only by lying flat with the knees flexed, a pillow under the back, and the head and neck supported. Any increase in the lumbar lordosis increases the pain, and high heels are uncomfortable. Going downstairs is harder than going up. If the patient jumps from a step he is often obliged to bend forward and to straighten up very gradually. The hip and lower leg motions are normal, as are also the reflexes and the skin sensations. The absolute diagnosis can be made only from the roentgenogram. The lumbarization of the first sacral vertebra may be much more pronounced on one side than on the other, or quite symmetrical on both sides, and the anomalies may be very complicated. In extreme cases the sixth lumbar or lumbarized first sacral vertebra appears almost suspended in the pelvis, and in these cases discomfort and pain may be very severe.

The Care and Cure of Crippled Children.—An editorial [52] in the *British Medical Journal* and a little book by Girdlestone [53] show how determined an effort is being made in Great Britain, especially in England, to ameliorate the condition of the cripple and provide for his complete rehabilitation. The British Central Committee for the Care of Cripples now supports 5,000 beds for this purpose. Twenty per cent of the forty counties have orthopedic clinics. The general plan includes a central hospital for the more acute and operative cases, accessory town clinics, and country fresh air hospitals for patients requiring heliotherapy, education and industrial training. Moreover, propaganda for the education of the medical and lay public has been started in order to combat the underlying causes of the diseases that produce crippling by inducing a general adoption of more hygienic methods of living.

52. Editorial, Brit. M. J., Dec. 12, 1925, p. 1133.

53. Girdlestone: Bristol, John Wright and Sons, 1925.

(*Concluded*)

CORRECTION

MECHANISM OF BACTERIAL INFECTION

In Dr. Wilensky's article on this subject, in the August issue of the ARCHIVES OF SURGERY, the legend for figure 3 was incorrect. It should have read: Fig. 3.—Comparison should be made with case 7 in the text.

Correspondence

"THE RELATION OF THE BONE MARROW TO THE LYMPATHIC SYSTEM"

In his article on the subject in the November, 1925, issue of the ARCHIVES OF SURGERY, Kolodny has suggested that the bone marrow is supplied with lymphatic channels, although this has been denied by a large number of writers, of whom I am an unrepentant one. He adduces a certain amount of evidence for his contention, and it seems to be necessary to point out that other interpretations of it are possible, and are, to my mind, more probable.

His evidence is obtained from the results of injection of India ink into the medullary cavity and subsequent recovery of it from "regional" lymphatic glands: this is admittedly a summary review of his admirable experiments, but it does, I think, bring out the essential principle. There is one question that immediately arises: Is there any good evidence that the India ink, which lodges in the local lymphatic glands, reaches them by way of lymphatic channels? It must be recollected that, if India ink is injected intravenously, some will be found in the lymphatic glands, and here there is no special reason for supposing that it has all arrived at this site after traveling along lymphatic channels. If, therefore, India ink can reach lymphatic glands from the blood stream, it is surely possible that this is the mechanism by which it did so in Dr. Kolodny's experiments. This is an even greater probability when it is recollected that the India ink was injected directly into the medullary cavity and not into any definitely known and recognizable channel.

The evidence obtained in this manner by Kolodny is amplified by reference to the process of metastasis of malignant epithelial tumors. He states that in mestastatic carcinoma of the bone veins filled with carcinomatous cells are easily found, but he does not mention that these may be found even inside the bone marrow, whereas intramedullary lymphatic channels filled with such cells have never been described. (Piney, A.: Brit. J. Surg. **10**:235 [Oct.] 1922; **11**:707 [April] 1924.)

I think that I am not misinterpreting Kolodny when I presume that he regards the deposition of carcinomatous cells in the bone marrow as being the result of permeation of the lymphatic channels. If this were really the case, it would not be possible to understand how such metastases could occur in association with extremely small early carcinomas, as is not infrequently the case. The description of invasion of bones by retrograde lymph flow from hypogastric lymph glands in cases of carcinoma of the prostate is not really convincing; many cases of bony metastasis in the femora (derived from a primary growth in the prostate) are on record, but the hypogastric lymph nodes are by no means invariably involved.

As in the preparation of jugged hare, it is essential first to catch the hare, in the present case it is necessary to find the lymphatic channel full of cancer

cells. Kolodny writes of Sampson Handley's lymphatic channels passing from muscle insertions to bones as being hypothetic, but the channels of which he himself writes are equally so; neither he nor Sampson Handley have seen the channels. The hematogenous origin of metastatic tumors of the bone seems to be sufficient explanation of the known facts, and did not William of Occam contend that "entia non sunt multiplicanda praeter necessitatem"?

A. Piney, M.D., London, England.